

ANTICONVULSANT ACTIVITY OF SULFOXIDES AND SULFONES

H. HOUSTON MERRITT, M.D.

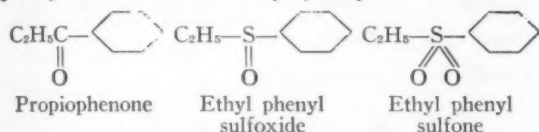
TRACY J. PUTNAM, M.D.

AND

W. G. BYWATER, Ph.D.

NEW YORK

Certain anticonvulsant sulfur compounds which were mentioned briefly in a previous publication¹ have been investigated in more detail. Interest in the possible anticonvulsant properties of the sulfoxides and sulfones was suggested by their structural similarity to the ketones, which had been found to have pronounced anticonvulsant activity.² These structural relationships are illustrated by the formula for ethyl phenyl ketone (propiophenone), ethyl phenyl sulfoxide and ethyl phenyl sulfone:



The sulfoxides and sulfones possess more desirable physical properties than the alkylaryl sulfides, which were also observed to possess anticonvulsant activity. Additional study of homologous sulfides was discontinued because of their undesirable odor and unsavory taste. Our interest in the sulfones was further stimulated by the observation that dimethyl sulfone occurs naturally.

Thus, Pfiffner and North³ isolated it from adrenal gland extracts, while Ruzicka and co-workers⁴ reported its isolation from dried cattle

From the Department of Neurology, Columbia University College of Physicians and Surgeons; the Montefiore Hospital; the New York Neurological Institute, and the Research Laboratories of Parke, Davis & Company.

1. Putnam, T. J., and Merritt, H. H.: Chemistry of Anticonvulsant Drugs, Arch. Neurol. & Psychiat. **45**:505-516 (March) 1941.

2. (a) Merritt, H. H., and Putnam, T. J.: A New Series of Anticonvulsant Drugs Tested by Experiments on Animals, Arch. Neurol. & Psychiat. **39**:1003-1015 (May) 1938. (b) Putnam and Merritt.¹

3. Pfiffner, J. J., and North, H. B.: Dimethyl Sulfone: A Constituent of the Adrenal Gland, J. Biol. Chem. **134**:781, 1940.

4. Ruzicka, L.; Goldberg, M. W., and Meister, H.: Inhaltsstoffe des Blutes: Isolierung von Dimethyl-Sulfon aus Rinderblut, Helvet. chim. acta **23**:559-561, 1940.

blood. Although this sulfone could arise from the metabolism of other naturally occurring sulfur-containing bodies, its occurrence in the animal organism aroused our curiosity about its possible biologic significance. It is also interesting to note that bis- β -hydroxyethyl sulfoxide has been found in adrenal gland extracts.⁵

EXPERIMENTAL STUDY

Method.—The sulfoxides and sulfones described in tables 1 and 2 were tested in cats by the method previously described.⁶ All the drugs were administered orally either in capsules or, if liquid, by stomach tube. The strength of current necessary to produce a convulsion was determined immediately before and approximately two hours after administration of the compound. The convulsive threshold for cats weighing 2 to 4 Kg. was usually 15 to 25 milliamperes. After administration of an effective anticonvulsant, such as diphenylhydantoin sodium or phenobarbital, this threshold was raised to over 50 milliamperes. In order to conserve animals, stimulations with currents in excess of 50 milliamperes were not given. The anticonvulsant action of a compound was rated for a particular dose as follows:

- O...No change in convulsive threshold
- +...Elevation of convulsive threshold 5 to 15 milliamperes
- ++...Elevation of convulsive threshold 20 to 30 milliamperes
- +++...Convulsive threshold elevated to 50 milliamperes
- ++++...Convulsive threshold elevated to more than 50 milliamperes
(i. e., no convulsion obtained when stimulated with 50 milliamperes)

In each instance tests were made at more than one level. When the compound was inactive, only the highest dose employed in the tests is

5. Reichstein, T.: Ueber Cortin, das Hormon der Nebennierenrinde, Helvet. chim. acta **19**:41, 1936. Reichstein, T., and Goldschmidt: Ueber die Bestandteile der Nebennierenrinde: III. Die schwefelhaltige Körper, ibid. **19**:401-402, 1936.

6. Putnam, T. J., and Merritt, H. H.: Experimental Determination of the Anticonvulsant Properties of Some Phenyl Derivatives, Science **85**:525-526, 1937. Merritt and Putnam.^{2a}

reported. The dose giving a + + + + response for the active compound is recorded, toxicity permitting. A typical example of the ranges in doses is given for *p,p'*-diaminodiphenyl sulfone and its diacetyl derivative.

TABLE 1.—Anticonvulsant Activity of Sulfoxides ($RSOR'$)

R	R'	Anticonvulsant Activity	Dose, Mg./Kg.
Ethyl	Phenyl	++++	70
n-Propyl	Phenyl	++++	150
Isopropyl	Phenyl	++++	150
		0	100
Phenyl	Phenyl	0	200
		+	250*
p-Nitrophenyl	p-Nitrophenyl	±	300
p-Phenetyl	p-Phenetyl	0	225

* Toxic dose.

TABLE 2.—Anticonvulsant Activity of Sulfones (RSO_2R')

R	R'	Anticonvulsant Activity	Dose, Mg./Kg.
Methyl	Methyl	0	70
Ethyl	Ethyl	0	130
Ethyl	Phenyl	++++	100
n-Propyl	Phenyl	++	520
n-Dodecyl	Phenyl	0	470
Ethyl	o-Aminophenyl	0	50
Ethyl	p-Aminophenyl	+	470
n-Dodecyl	p-Aminophenyl	0	450
Phenyl	p-phenyl	±	370
Phenyl	p-Aminophenyl	0	520
		0	112
		0	178
p-Aminophenyl	p-Aminophenyl	+	185
		++++	227
			357*
p-Aminophenyl	m-Aminophenyl	++	500
		0	217
p-Acetaminophenyl	p-Acetaminophenyl	0	250
		0	400
p-Acetaminophenyl	p-Nitrophenyl	0	500
p-Tolyl	p-Tolyl	0	260
p-Aminophenyl	o-Sulfonamido-p-aminophenyl	0	800
p-Aminophenyl	2-Amino-5-thiazolyl	++++	170†
		0	70
Ethyl	2-Benzothiazyl	0	150*
Phenyl	CH ₂ CONH ₂	0	460
Phenyl	CH ₂ CH ₂ CONH ₂	0	470

* Lethal dose.

† Dose dissolved in diluted hydrochloric acid and administered by stomach tube.

Results.—Unfortunately, dimethyl sulfone was inactive in the dose tested, and the experiment did not help to elucidate the pharmacologic significance of this sulfone in the animal organism. We believe the given dose was large as compared with the probable concentration of dimethyl sulfone (about 375 mg. per thousand kilograms of dried cattle blood)⁵ in the animal body and therefore some response might have been expected if the drug were acting on the mechanism involved in this anticonvulsant test.

The peak of activity in the sulfoxide and sulfone series studied occurred with the alkylaryl derivatives. Thus ethyl phenyl, propyl phenyl and isopropyl phenyl sulfoxides and the ethyl phenyl and propyl phenyl sulfones are active. The activity apparently drops off with *n*-propyl

phenyl sulfone and is entirely lacking in dodecyl phenyl sulfone. Introduction of an amino group into ethyl phenyl sulfone, either in the ortho or in the para position, destroyed the activity of the parent compound.

Diphenyl sulfoxide and diphenyl sulfone were only slightly active. Introduction of one amino group into the latter compound did not increase the activity, but two amino groups symmetrically substituted results in greater activity (*p,p'*-diaminodiphenyl sulfone). However, the diaminodiphenyl sulfone was not as active as the alkylaryl sulfoxides or ethyl phenyl sulfone.

A comparison of the more promising sulfoxides and sulfones with the corresponding ketones is shown in table 3. The figures in parentheses denote the oral dose in milligrams per kilogram at which the activity was found.

TABLE 3.—Comparative Anticonvulsant Activities of Sulfoxides and Sulfones and Ketones*

R	R'	Ketone	Sulfoxide	Sulfone
Ethyl	Phenyl	++++ (300)	++++ (70)	++++ (100)
n-Propyl	Phenyl	++++ (330)	++++ (150)	++ (520)
Phenyl	Phenyl	++++ (200)	± (250)	± (370)
p-Aminophenyl	p-Aminophenyl	0 (200)	..	++++ (227)

* Figures in parentheses represent the oral dose, expressed in milligrams per kilogram of body weight, at which the activity was found.

Ethyl phenyl sulfone was chosen for clinical trial because it is the most stable and easily prepared of the active drugs in this group. It does not have the sedative action of propiophenone, and, as a low-melting solid rather than a liquid, it is more easily administered. Acute and chronic toxicity studies on mice, rats and dogs show it to be somewhat more toxic than diphenylhydantoin sodium but suitable for clinical use in low doses.⁷

CLINICAL RESULTS WITH ETHYL PHENYL SULFONE

Twenty patients refractory to other forms of treatment have been treated with ethyl phenyl sulfone for periods of one to eighteen months in doses varying from 0.2 to 1.6 Gm. per day. It can readily be seen from table 4 that ethyl phenyl sulfone was effective in the treatment of convulsive seizures in certain patients. In spite of the fairly large doses which have been used, there have been no serious untoward effects. In fact, the drug produced practically no symptoms.

CASE 1.—S. G., a 22 year old white man, had been subject to grand mal attacks and minor seizures, char-

7. Dr. O. M. Gruzhit, of Parke, Davis & Company, furnished the data on toxicity.

acterized by falling to the floor without apparent loss of consciousness, since the age of 14. Grand mal seizures occurred once every four to five days. Treatment with diphenylhydantoin sodium was started in February 1938. After a few months' treatment, the dose of this drug was increased to 0.6 Gm. a day. The number of grand mal attacks was reduced to one until early in 1940, when the minor attacks began to occur with greater frequency, until they numbered one to several daily. The addition of phenobarbital (3 grains [0.195 Gm.] a day) or phemitone (3-methyl-5-phenyl-5-ethyl barbituric acid) (6 grains [0.39 Gm.] per day) to the dose of diphenylhydantoin was not followed by any decrease in the frequency of attacks. In October 1941 ethyl phenyl sulfone, in a dose of 0.8 Gm. per day by mouth, was added to the dose of 0.5 Gm. of diphenylhydantoin sodium, and to May 1943 there were one grand mal attack and six of the minor attacks. During this period the patient had taken a job as

1942, June 1942, October 1942 and April 1943. After the patient's father died, in June 1943, she was sent to a special school, where she was treated by the school physicians. During treatment with ethyl phenyl sulfone there were no signs of toxicity. Periodic blood counts and examinations of the urine gave normal results. There had been a reduction in weight from 130 to 115 pounds (65 to 57.5 Kg.), as a result of dieting for obesity.

CASE 3.—M. S., a 15 year old white girl, had been subject to grand mal seizures since the age of 14 months. These seizures occurred on an average of once a week in spite of administration of phenobarbital and bromides and a ketogenic diet. Diphenylhydantoin sodium therapy was started in December 1937 but was discontinued after the appearance of a cutaneous rash. From 1937 to 1942 the patient was treated with various combinations of diphenylhydantoin, phenobarbital,

TABLE 4.—Effect of Ethyl Phenyl Sulfone on Convulsive Seizures

	Color	Sex	Age, Yr.	Dose, Gm.	Length of Time Administered, Months	Effect on Frequency of Seizures as Compared with Previous Forms of Treatment	General Condition of Patient	Signs of Toxicity
S. B.	W	M	22	0.7-1.2	24	Greatly decreased for 18 months	Improved	None
D. B.	W	F	16	0.3-1.0	21	Greatly decreased for 18 months	Improved	None
M. S.	W	F	15	0.8-1.2	11	Greatly decreased for 4 months	Improved	None
W. L.	W	M	21	0.8-1.2	6	Greatly decreased for 3 months; then same frequency as before	Unchanged	None
H. B.	W	M	21	0.8-1.2	12	Greatly decreased	Unchanged	None
F. C.	W	M	26	0.6-1.0	3	Unchanged	Unchanged	None
D. A.	N	F	4	0.2-0.4	2	Unchanged	Improved	None
E. C.	W	F	30	0.2-1.0	4	Slightly decreased	Unchanged	None
G. L.	W	M	14	0.8-1.6	6	Moderately decreased	Improved	Slightly ataxic on large dose
C. L.	W	M	43	0.8-1.4	3	Slightly decreased	Unchanged	Slightly ataxic on large dose
V. M.	W	M	11	0.4-1.0	12	Slightly decreased	Unchanged	Slightly ataxic on large dose
J. N.	W	M	14	0.4-1.4	7	Unchanged	Unchanged	None
N. P.	W	M	7	0.4-0.8	2	Unchanged	Unchanged	None
J. P.	W	M	16	0.3-1.2	4	Unchanged	Unchanged	Slight gastric distress
F. S.	W	M	8	0.3-1.0	4	Unchanged	Unchanged	None
I. W.	W	F	35	0.2-1.0	9	Decreased	Unchanged	None
S. S.	W	F	12	0.5-1.0	1	Unchanged	Unchanged	None
C. R.	W	F	5½	0.2-0.6	1	Unchanged	Unchanged	None
J. C.	W	M	44	0.2-1.0	3	Unchanged	Unchanged	None
G. E.	W	F	12	0.4-1.2	4	Slightly decreased	Unchanged	None

attendant in a hospital and had worked regularly. In October 1943 the minor attacks began to recur at intervals of five to seven days, and ethyl phenyl sulfone was discontinued. While the patient was taking the drug, periodic examinations of the urine and blood gave normal results. The weight has remained stationary, and there have been no signs of a toxic effect of the drug.

CASE 2.—D. B., a 16 year old white girl had been subject to grand mal seizures since the age of 7 years. Attacks occurred about once every two to three weeks. Previously she had been treated with large doses of phenobarbital (4½ grains [0.29 Gm.] a day), diphenylhydantoin sodium (0.5 Gm. a day) and combinations of diphenylhydantoin and phenobarbital, phemitone or bromides. Treatment with ethyl phenyl sulfone, 1 Gm., and diphenylhydantoin sodium, 0.4 Gm., was started on Sept. 19, 1941. Subsequent attacks occurred February

phemitone and bromides, with no appreciable reduction in the frequency of the attacks. In October 1942 treatment with ethyl phenyl sulfone, in a dose of 1 Gm. a day, and phemitone, in a dose of 0.1 to 0.2 Gm., was started. The patient had no attacks for eight weeks and only three attacks in the next three months. After this the attacks began to recur at intervals of ten to fourteen days, and ethyl phenyl sulfone was discontinued in September 1943. There were no toxic symptoms while the patient was taking the sulfur compound. The blood and urine were normal, and there was no change in weight.

No attempts were made to determine the effect of the drug on patients whose seizures have been controlled by either phenobarbital or diphenylhydantoin, because it was believed that any new drug should be subjected to the more severe test

first and proved to be superior to the drugs in common use in treatment of the refractory conditions before it is recommended for the less refractory ones.

SUMMARY

A series of sulfoxide and sulfone drugs have been studied for their anticonvulsant effect in the cat, using the electric shock technic.

Ethyl phenyl sulfoxide and ethyl phenyl sulfone raise the convulsive threshold in doses

comparable to the dose of propiophenone without producing a hypnotic effect.

Clinical trial of ethyl phenyl sulfone indicates that it has definite anticonvulsant activity, but this activity is not sufficiently greater than that of diphenylhydantoin sodium to recommend it for general use on the basis of the preliminary appraisal.

Mr. B. F. Tullar and Mr. L. L. Bambas prepared the sulfoxides and sulfones.

Montefiore Hospital for Chronic Diseases.

Poly
on foc
mon c
to tha
two in
toms r
and v
duce
of the
ular c
planat
the p
sion
merel
before
An
ular
reduc
scribe
strab
patien
this
diplo
origin
at 6
with
ing p
macu
ocula
were
quen
two
this
Ca
Fr
Calif.
T
Divis
Surge
views
and a
polic
1.
Opht
2.
Mon
3.
ohne
das S
4.
Case

POLYOPIA AND MONOCULAR DIPLOPIA OF CEREBRAL ORIGIN

COMMANDER M. B. BENDER, MC(S), U.S.N.R.

Polyopia, or the seeing of multiple images on focusing on one object, is a relatively uncommon condition. This optical illusion is allied to that of monocular diplopia, or the seeing of two images with one eye. Although these symptoms may be found with hysteria, there are many and varied organic conditions which can produce formation of multiple images.¹ Diseases of the ocular media are known to produce monocular diplopia or even polyopia. Here the explanation involves a simple consideration of the physics of light and optics.² The same illusion can be reproduced in the normal subject merely by placing an appropriate lens or prism before the intact eye.

Another seemingly peripheral cause of monocular diplopia is strabismus, with resultant reduction in visual acuity. Bielschowsky³ described the case of a man who had convergent strabismus and amblyopia in the left eye. The patient lost his normal, right eye, and after this he suffered from troublesome monocular diplopia. Vision in the remaining eye, which originally was reduced to ability to count fingers at 6 meters, improved when he learned to fix with the congenital macula. During this learning period, the patient used not only the true macula but the false macula produced by the ocular strabismus. Thus these two foveal points were stimulated at different times. Consequently in the foveal "area" there developed two "space values" for each retinal point, and this resulted in persistent diplopia.

Cass⁴ found that 33 of 70 patients with squint

had monocular diplopia under certain conditions. He elicited the diplopia by stimulating the abnormal, or "eccentric," fixation point (false macula) in the squinted eye, which corresponded to the true macula of the normal eye. He explained the monocular diplopia on a psychologic basis and stated that it was caused by bringing into consciousness simultaneously the retinal "space values" of the congenital (true) macula and of the acquired (false) macula.⁵ In his discussion, Cass considered the relationship between the eye and the body image to objects in space. To a certain extent, the development of one's orientation of objects in space with regard to one's own body during the act of vision depends on the combination of sight and other sense modalities.

Monocular diplopia has also been noted in patients who have involuntary tonic deviation of the eyes due to lesions of the cerebellum or disease of the vestibular mechanisms and in persons who have difficulty in convergence.⁶ In some cases it may be present when the eyes are deviated in the extreme lateral position (either with or without nystagmus in such position). However, the monocular diplopia in these conditions is transitory and depends largely on the position of the eyes. Uniocular diplopia and binocular triplopia have been found in patients with lesions of the pituitary implicating the optic chiasm. In these patients a large vertical scotoma situated in the midportion of the field of vision of one eye may be found.⁷

Lesions of the occipital lobe or of the central visual pathways may also produce monocular diplopia and polyopia. The etiologic factors are varied. Encephalitis, multiple sclerosis, trauma

5. Each retinal point has a definite orientation in space with regard to the macula. In turn, each retinal point has a functional "space value" corresponding to the "space value" of a retinal point in the other eye.

6. (a) Klein, R., and Stein, R.: Ueber einen Tumor des Kleinhirns mit anfallsweise auftretendem Tonusverlust und monokulärer Diplopie bzw. binokulärer Triplopie, *Arch. f. Psychiat.* **102**:478-492, 1934. (b) Gerstmann, J., and Kestenbaum, A.: Monokuläres Doppeltsehen bei cerebralen Erkrankungen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **128**:42-56, 1930.

7. Author's personal observation in 3 cases.

From the United States Naval Hospital, San Diego, Calif.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as official or reflecting the policies of the Navy Department.

1. Pincus, M. H.: Monocular Diplopia, *Am. J. Ophth.* **24**:503-506, 1941.

2. Verhoeff, F. H.: The Cause of a Special Form of Monocular Diplopia, *Arch. Ophth.* **29**:565-572, 1900.

3. Bielschowsky, A.: Ueber monokuläre Diplopie ohne physikalische Grundlage nebst Bemerkungen über das Sehen Schielender, *Arch. f. Ophth.* **44**:143, 1898.

4. Cass, E. E.: Monocular Diplopia Occurring in Cases of Squint, *Brit. J. Ophth.* **25**:565-577, 1941.

and tumor are some of the diseases which have been mentioned.^{6b}

Hoff and Pötlz⁸ reported the case of a 49 year old man who had monocular diplopia and, later, polyopia as a result of tumor in the right occipital lobe. This they explained by a stretching of the occipital cortex in its polar extremity. They proposed the theory that polyopia is the result of concomitant tendencies of two visual functions interfering with each other: the attempt to fixate the object is hampered by forced conjugate deviations of the eyes. Fixation is faulty, owing to the involvement of the occipital pole, and the impulse to deviate is due to irritation of the occipital cortex.

Goldstein,⁹ in an interesting paper, described 3 cases of monocular diplopia. Two of the patients had disturbances in the field of vision, while the third patient, with a lesion of the posterior fossa, had abnormal tonic pull in the muscles of the eyes. The author explained the monocular diplopia in the first 2 cases on the following basis: In the attempt to overcome a poor visual performance, the main visual image is displaced to an area where the threshold is normally better, as toward a new fovea. Sometimes the patient sees only the displaced image, but at other times he experiences the first stimulus in addition, so that he sees double. This explanation is somewhat similar to interpretations offered by Bielschowsky³ and Cass.⁴ As for monocular diplopia, in his third case, in which apparently there were no changes in the visual fields, Goldstein argued that the patient, in his effort to overcome the abnormal tonic pulling of the eyes, may maintain fixation on an object only with consequent diplopia. Goldstein further stated that these reactions represent the organism's best possible performance under abnormal conditions. Rather than suffer from blurred vision, the patient manages to see a clear image even though it appears double; diplopia is the "price" the organism has to pay in order to improve the bad vision caused by faulty fixation.

The diplopia in either case is accomplished by a "diffusion" of the visual image after it reaches the cortex. This abnormal "diffusion" of an excitation leads to a spreading of the image perceived, involving areas in the visual cortex which have different "space values." At this point in

the process of "diffusion" a new image forms about a new "spatial value," while the old one persists, thus producing two images differing in clarity and intensity. The more foci are involved by the diffusion, the more images are perceived, thus leading to polyopia.

This interpretation seems plausible, but the part of his theory which is difficult to accept is the notion of "diffusion." Although Goldstein referred to some of his older work, there is insufficient proof that "diffusion" of an excitation in the cortex is a principle which is generally recognized in physiology or psychology, unless by diffusion he means the phenomenon of irradiation. Apparently, Goldstein used the term "diffusion" in a pathologic sense, as a disturbance in "figure-ground" formation.¹⁰

"Diffusion" thus appears to be an inferential concept. On the other hand, observations on patients with a pseudofovea¹¹ confirm the contention of Goldstein and other earlier investigators that new cortical space values may emerge in such cases and may at times create conflict in the patient's organization of visual space. The question then raised is: How and in what circumstances are such new space values activated? This may be partly answered by studying the following cases.

REPORT OF CASES

CASE 1.—D. G. H., a 20 year old Marine, corporal, was wounded in the back of his head by shrapnel. This rendered him unconscious. When he recovered, shortly thereafter, he found he was totally blind and had a humming noise in the ears. He remembered he heard voices, which seemed to be distant. Within a few hours after he was injured a craniotomy was performed, and a large gaping wound was noted in the occipital bone. A piece of the calvaria 1½ inches (3.7 cm.) in diameter was found to be depressed below the inner table on the left side. On elevation of the fragment of bone, the dura was observed to be torn, and the underlying brain tissue appeared to be "pulsed." After appropriate surgical manipulation, the wound was closed, and the patient was evacuated from the combat area. Aboard ship,

10. The term "figure" and "ground" in the usage of Gestalt psychology denotes a general principle of organization of visual perception. During the act of perception the "figure" is represented in the cortex by an area of highest excitation, while the surrounding area of excitation represents the "ground" of the percept. Goldstein assumed that under pathologic conditions the distinctness of the "figure" may be decreased by an abnormal spread or diffusion of excitation on the "ground."

11. Kanzer, M., and Bender, M. B.: Spatial Disorientation with Homonymous Defects of the Visual Field. *Arch. Ophth.* **21**:439-446 (March) 1939. Bender, M. B., and Kanzer, M. G.: Dynamics of Homonymous Hemianopia and Preservation of Central Vision, *Brain* **62**:404-421, 1939. Bender, M. B., and Furlow, L. T.: Visual Disturbances Produced by Bilateral Lesions of the Occipital Lobes with Central Scotomas, *Arch. Neurol. & Psychiat.* **53**:165-170 (March) 1945.

8. Hoff, H., and Pötlz, O.: Zur diagnostischen Bedeutung der Polyopie bei Tumoren des Occipitalhirnes. *Ztschr. f. d. ges. Neurol. u. Psychiat.* **152**:433-450, 1935.

9. Goldstein, K.: Ueber monokuläre Doppelbilder: Ihre Entstehung und Bedeutung für die Theorie von der Funktion des Nervensystems, *Jahrb. f. Psychiat. u. Neurol.* **51**:16-38, 1934.

and on the second postoperative day, convulsions were noted. These seizures, jacksonian in character, were present periodically for over eight days.

For a short while he had signs of increased intracranial pressure, but despite this he improved. On the fifteenth postoperative day, a cursory examination disclosed that, although he had recovered his vision, homonymous hemianopsia remained. There were no other notations as to his visual symptoms. However, when the patient was interviewed, two months after the injury, the following history was obtained:

For the first three or four days he was completely blind. Then perception of light returned, and everything before him appeared gray and blurred, as if he were looking through a fog. He appreciated motion but could not recognize form. He was not aware of objects, nor could he detect them unless they were in motion.

Polyopia and Diplopia.—On or about the seventh or eighth day after the injury, he began to recognize the form of objects, but these appeared to be multiple. Everything around him seemed to be quadruple, no matter in what direction he looked. The four images were arranged in two parallel pairs, one above the other. Everything seemed to be indistinct, and he was unable to differentiate the true from the false images. They all appeared to be of the same size. At a near point the illusionary figures seemed to overlap, and as the object he was regarding moved away from him the images became rapidly smaller. He also found that on turning his head to one side all the images tended to move in the opposite direction and that when he laid his head on the side they tilted but kept in multiples of four, with one pair above the other. This multiple vision made him feel nauseous and dizzy, and, to avoid the uncomfortable sensations, he kept his eyes closed most of the time. He was unable to adjust to this quadruple vision, which he had for five days. After this he noticed that his sight was somewhat better and that the vision became double when he looked in certain directions, as on turning his head to the right.¹² At that time he could differentiate the true from the false image. The diplopia was only in the horizontal meridian, whereas the quadruplopia was along the vertical and horizontal meridians.

He continued to improve. On about the seventeenth day after the injury, the quadruple vision disappeared, and he had only diplopia. Subsequently, he noted that if he turned to the right or viewed objects with his left upper field of vision, the image appeared to be clear and single. All around this "clear spot" he said objects were "blurred and double." Thus, if he sighted a string suspended in the left upper field of vision, part of the string was clear and single, while the rest was blurred and double. On about the twenty-seventh day after the injury, his vision was much improved, and he no longer had the illusion of multiple images. There were no hallucinations.

Disturbance in Space Perception.—As soon as he was able to recognize the form and shape of objects, he found he had difficulty in reaching for food on the tray or for toilet articles not only because of the polyopia but because he overshot his mark. On several occasions he thought he was speaking to some one far away, but actually the person was nearby.

12. Ocular muscle paresis could not be excluded, since the patient did not know whether the diplopia was binocular or monocular. He did not test his vision with one eye covered.

Perception of Time.—Time seemed to pass very quickly. What appeared to him to be a few days turned out to be a few weeks. He felt that objects tended to move away from him at a rate much faster than the ordinary. Thus, he found that as the nurse walked away from the bed, she reached a distant point in a much shorter period than he expected.

Perception of Color.—The ability to appreciate color did not return until about twelve days after he began to see light. During this period objects appeared gray and generally indistinct.

Other Temporary Symptoms.—Besides the visual disturbance, he had slight difficulties in calculation, spelling, reading and writing and showed other fragments of aphasia. These symptoms were present only to a minimal extent and disappeared completely four months after the injury.

Past History.—The past medical and social histories were noncontributory. He had completed but two years of high school. He had always been mild mannered, calm and phlegmatic. He denied having a preenlistment anamnesis of neurotic traits and reactions.

Physical and Neurologic Examination.—His condition was essentially normal except for the healed wound over

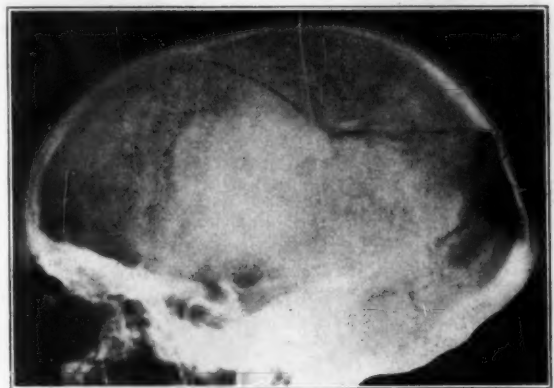


Fig. 1 (case 1).—Roentgenogram of the skull, illustrating the defect in the left occipital bone produced by the shrapnel wound and operation for removal of fragments of bone.

the occiput, a hearing defect on the left side and the visual disturbances, to be described later. A roentgenogram of the skull revealed a circular defect 4.5 by 5 cm. in the left occipital bone, with four radiating fracture lines (fig. 1).

Special personality and psychologic tests failed to disclose significant neurotic trends.

The retina, optic nerve and macula of each eye appeared normal. The movements of the ocular globes were full, and there was no evidence of latent paresis with the red glass test. Ability to fuse images and stereoscopic vision were normal when tested six months after the injury. There was no nystagmus. The pupils were equal and reacted well to light and in convergence. Opticomotor nystagmus was found when the revolving striped drum, held vertically before the eyes, was rotated to the left or to the right. When the drum was held horizontally and rotated downward, there was normal nystagmus, but not when it was rotated upward. The dark adaptation time was seven and one-half minutes on the Feldman adaptometer. (The highest normal value on this instrument is five minutes.)

Perimetric examination for motion disclosed defects in all but the left homonymous superior quadrants of the fields of vision (fig. 2A). The defects appeared to be incongruent. The exact border of the area for complete loss of perception for motion could not be plotted with any degree of certainty, for within the zone of indistinct vision (stippled area) there were islands of complete blindness. However, these scotomas were inconstant and on several occasions tended to assume a circular shape, an incomplete "ring scotoma." On the tangent screen, the scotomatous changes about the fixation point were more clearly demonstrated (fig. 2B).¹³

Tachistoscopic Examination.¹⁴—With one-tenth second exposures, these tests disclosed marked weakness in perception, particularly in the defective visual quadrants. At this speed the patient also showed difficulty in recognition of color. Reduction in the speed of exposure did not materially improve his perceptive abilities. Re-examination with one-tenth second exposures, repeated

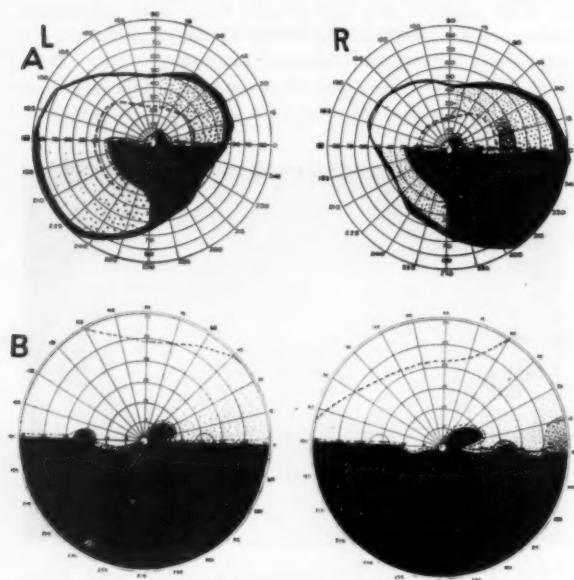


Fig. 2 (case 1).—Fields of vision as plotted on the perimeter (A) and the tangent screen (B) with a test object 5 mm. in diameter, an illumination of 7 foot candles and a distance from the fixation point of 33 cm. Solid black areas represent loss of perception of motion, and stippled areas, loss of recognition of form and color for objects of 5 mm. diameter. In this figure, and in figure 5, the degree of impairment is indicated by the size and density of the dots. The area within the line of dashes indicates preservation of color. The fields are incongruent. In the temporal field of the right eye there appeared to be a transient ringlike zone of defective vision.

five months after the injury, revealed improvement in perception of form and color and in interpretation of exposed drawings of familiar objects. With short exposures the patient was able to detect figures in areas

13. Examination was performed under 7 foot candles of illumination at a distance of 35 cm., and a 5 mm. test object was used. Visual acuity was 20/20 in each eye.

14. The examination was performed in a dark room with images flashed on a screen, on which the patient fixated on a central point from a distance of 5 feet (152 cm.),

which seemed to be deficient for recognition of form, and even motion, when tested on the tangent screen or with one or two second exposures on the tachistoscopic screen.

Visual After-Image.—The after-image the patient had was usually incomplete, inasmuch as he could see only the left upper portion of an object on which he was fixing. Thus, after fixing for thirty seconds on the star in the right lower corner of the American flag painted in green, black and yellow, the negative after-image he saw on a white background was in complementary colors. However, he saw only parts of the flag—the blue field with white stars and one or two red and white stripes below the field. The rest of the flag was not visualized in the after-image. The fixation was made at a distance of 10 inches (25 cm.). When he fixated on the flag at a greater distance, such as 20 inches (50 cm.), the after-image was more complete. He then visualized all but the right lower quadrant. Apparently, he had an after-image of a part of the field of which he was not aware with the ordinary tests, such as the tangent screen or the perimetric test. The same after-imagery responses were obtained when he closed his eyes after thirty seconds of fixation on the star. The after-image obtained in this manner appeared to be much smaller and to be more intensely colored on a black background. Again, the area of the after-image was more extensive than that which he saw in the plotted visual fields.

When he fixated on a light (100 watt bulb behind a convex lens) 3 inches (7.6 cm.) from his eyes for five seconds and then closed his eyes, the after-images he saw appeared within seven seconds and continued with changing colors, from yellow to blue to green to red, for two minutes thereafter. The results obtained were the same in each eye. Evidently, in this test, he showed no deviation from the normal except that on several occasions the shape of the image varied.

Fluctuation, Obscuration and Extinction of the Visual Images.—When the patient fixated on the flag, he claimed that at first it seemed as though he saw the entire flag; but when he concentrated on the star, the part of the flag on his right side seemed to have "blackened out," and the rest of the area around the fixation point tended to become gray and to fluctuate in distinctness. When he was asked to fix on a dot about which were drawn four vertical lines, one line being situated in each of the four quadrants about 1.5 cm. from the fixation point, it was noticed that within two to three seconds the line in the right upper quadrant disappeared; the line in the left lower corner (area of defective vision) waxed and waned at a fluctuating rate, the image being present for seven or eight seconds and absent for one or two seconds. These phenomena have been previously described in patients with lesions in the visual pathways.¹⁵

When he fixated on a central point, it was noticed that he could immediately recognize a large object, such as a pencil, in the right upper quadrant 10 to 15 degrees from the fixation point. However, within five seconds the image of the pencil began to wax and wane, and several times he could not perceive it at all, the image becoming totally extinct. This visual fluctuation, obscuration and transient extinction were not evident in the left superior quadrants of vision. There the object regarded showed only slight fluctuation. On looking

15. Bender, M. B., and Furlow, L. T.: Phenomenon of Visual Extinction in Homonymous Fields and Psychological Principles Involved, *Arch. Neurol. & Psychiat.* 53:29-33 (Jan.) 1945.

in a mirror he usually saw his face; but when he fixated at the bridge of his nose, everything below the nose and to the right seemed to be gone and the space was gray. The observation made here conformed to the results with the tachistoscope, for during a rapid exposure the patient seemed to see objects in apparently defective areas about the central field. He showed no difficulty in recognizing hues and tones of color. There was no sign of defective visual memory and no apparent spatial disorientation at these examinations. He also denied ever having had visual hallucinations.

Examinations on the perimeter and the tangent screen repeated five months after the injury revealed a slight contraction in the extent of the scotoma originally found in the right upper and left lower quadrants of the field of vision.

Comment.—It is interesting to note that as the patient's vision improved the polyopia became less apparent and changed into diplopia. This was particularly noticeable at the time when the patient found that on turning his head and eyes in certain directions, especially to the right, vision was better.¹⁶ Evidently, in order to see better, the patient made use of his mechanisms for ocular fixation.

In this zone of improved vision there was diplopia, whereas the rest of the field seemed to present four images. Thus, there were two types of multiple image formation, expressing two degrees of severity of the same functional disturbance. Moreover at a later date, when the patient had only double vision, he found that by turning his head he localized an area of clear and monocular vision. This was on his left side. Apparently, as soon as visual perception improved, the polyopia disappeared. Unfortunately, the patient did not test his visual abilities with one eye closed; so it cannot be stated whether or not he had monocular diplopia or double vision due to inability to fuse images or to palsy of an ocular muscle. However, since he had polyopia and since the diplopia had a similar localization in the field of vision, it is assumed that the formation of double images was of cerebral origin, and probably monocular.

Significant and important were the fluctuation, obscuration and extinction of the perceived image. This phenomenon is known to produce a disturbance in the mechanism of fixation. Such a disturbance might play a role in the formation of multiple images. Also significant was the fact that in one plane, such as that of the suspended string, the patient had a zone of single and clear vision, with double, blurred vision above this zone.

Another interesting symptom presented by this patient was a spatial disorientation in his remain-

ing field of vision. Such a visual disturbance, which was described by Riddoch¹⁷ and Brain,¹⁸ might be associated with dysfunction in the mechanism of fixation or be caused by a derangement in the space values about a focal visual point.

In the following case, the syndrome of polyopia, spatial disorientation and difficulty in fixation is again noted.

CASE 2.—E. McL., a 22 year old Marine, sergeant, was wounded in the right occipital area by enemy machine gunfire. He lost consciousness for a moment or so, and when he recovered he found he was completely blind. Two hours after the injury his sight began to return and he perceived light. Everything appeared blurred. He had a "feeling" that he could not see or look upward. A few hours later, after his head wound was dressed, his sight improved rapidly, but since then his vision had never seemed normal to him.

Spatial Disorientation.—For the next five days he was unable to judge distances properly and he could not fixate on an object. In eating he had difficulty in handling the food because he could not gage the distance between the plate and his mouth. He usually fell short of his mark. He also had trouble in estimating the location of an object in space. For instance, on walking through the hatchway of a ship, he was unable properly to judge the position of the door. At this time, he was able to write a letter. He could see the form and shape of an object, although he could not always recognize it.

Polyopia.—At first he found he was unable to read or to write because of formation of blurred and multiple images. As he focused on any object he was regarding, the perceived image became blurred. It waxed and waned; and the more he tried to distinguish it the more it tended to become double, and within a few seconds it spread in a horizontal row to his right to become multiple. The multiple images were parallel, close to one another and all of the same size. The row formed a somewhat oblique line, with the images on his right somewhat higher than those on his left. The illusion always developed to his right, and often he felt as if he were turning his eyes or they were being pulled to the right so as to follow the images. This made him feel dizzy, and he had discomfort in his eyes.

The images were generally indistinct and had little color. The farther the object was from him, the dimmer it appeared and the less he could distinguish, even though there were many images. Closing the eyes for a few seconds or just gazing into space without fixation would abolish the illusion. Also, when he turned his eyes back to the left or to the original object, the polyopia would disappear. The polyopic experiences lasted four days, and for the next six days he saw only double when he fixated on an object. At this time the vision and images were not nearly as blurred as when he saw multiple. The diplopia was present directly before him, but the double images "moved to the right"

17. Riddoch, G.: Visual Disorientation in Homonymous Half-Fields, *Brain* **58**:376-382, 1935.

18. Brain, R.: Visual Disorientation with Special Reference to Lesions of the Right Cerebral Hemisphere, *Brain* **64**:244-272, 1941.

16. By turning his head and eyes to the right, the patient viewed objects with his left field of vision.

in the same manner as in the case of multiple image formation.¹⁹

Fluctuation of Visual Image.—After the diplopia disappeared, he noticed that the waxing and waning of visual images became more apparent. For this reason, he had great difficulty in reading and writing. He found he was forced to close his eyes frequently or to stop reading so as to avoid a "running together" of the printed or written letters and words. With rest his vision became clear, but when he resumed reading the blurring recurred. Associated with the blurring, he felt a sensation of pulling and turning of his eye to the right. These symptoms lasted eight days and disappeared. Except for slight blurring of vision on fixation he was practically asymptomatic, and one month after he was injured he was returned to duty.

He participated in another invasion and returned with his outfit for a rest. Two months after the injury, he noticed that flexion of the neck produced unpleasant vibratory sensations in the lower part of the trunk and hips, radiating to the inner aspect of the thighs. Later, he found that the vibratory sensation rapidly spread into the toes. Subsequently, the upper extremities became affected. He also noted that when he accidentally bent his head while hiking he not only had the vibratory sensation through the body but felt strange in his feet, with a tendency to lose his sense of balance and to stagger. Because of these symptoms he was readmitted to the hospital.²⁰ Recently, he had found that tapping of the neck or acute flexion would produce a transient sensation of flickering light in both eyes, as if the eyes were opening and closing.

The physical examination revealed an essentially normal condition except for a healed scar over the right occipital region. A roentgenogram of the skull revealed three metallic fragments, each measuring about 0.5 cm. in diameter, in the right occipital area. Underlying this



Fig. 3 (case 2).—Roentgenogram of the skull, illustrating the defect produced by a bullet wound in the right occipital region.

scar was a spherical bone defect 1.5 cm. in diameter (fig. 3). An audiometric record disclosed 40 per cent deafness for higher tones in the right ear.

19. This patient, too, did not test his vision, with one eye closed, so that it could not be established whether he had monocular or binocular diplopia.

20. Similar complaints of dysfunction referable to the spinal cord have been noted in a number of other patients with gunshot wounds of the brain, as far forward as the frontal lobe. In these patients there were no other symptoms or signs of involvement of the spinal cord, nor was there injury anywhere but in the brain.

The results of neurologic examination were essentially normal except for a vibratory sensation in the trunk and extremities whenever the neck was flexed acutely. The fundi were normal. The pupils were equal and reacted well to light and in accommodation. The ocular movements were normal. Examination of the visual fields revealed a distinct scotoma in the left homonymous superior quadrant (fig. 4).

Fluctuation and Obscuration of Vision.—On fixating at a point with either one or both eyes, the patient complained that objects or figures in his left upper field of vision waned and waxed and that they became obscure and at times disappeared entirely. Thus, a pencil or a watch placed in that area would fluctuate in distinct-

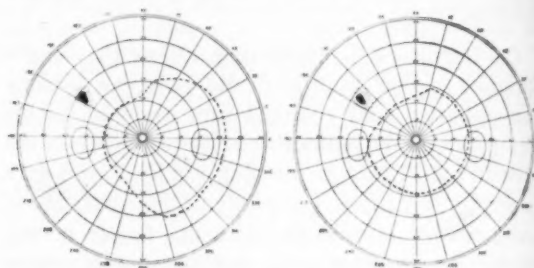


Fig. 4 (case 2).—Visual fields plotted on the tangent screen, illustrating a small scotoma in the left homonymous fields. Objects placed in the left field of vision fluctuated in their appearance, and with double simultaneous stimulations the image became obscure.

ness, become blurred and ultimately disappear from sight. At this time, he felt a pulling in his eyes, and he was unable to maintain his fixation. Also, the introduction of a simultaneous stimulus in his right field of vision would make the image in his left field become dimmer and more indistinct (obscuration phenomena).¹⁸

After-Imagery.—All responses seemed to be normal for form and color with both light and dark backgrounds. Dark adaptation time was five minutes on the Feldman adaptometer, a normal value. Tests for color vision gave normal results.

Tachistoscopic Test.—The patient seemed to show a decrease in perception with one-tenth second exposures, with weakness in his left upper field of vision, but this was not pronounced.

Comment.—This case is another example of polyopia and diplopia due to a lesion in the occipital lobe. Here, however, the polyopia was along the horizontal meridian, with slight tilting. The illusion developed to the right and seemed to be associated with a forced ocular deviation. As the patient fixated on the object, the image blurred, and he felt as if the eyes pulled to the right. This phenomenon was soon followed by progressive increase in the number of false images to the right. It seemed to him that in order to follow the extra images his eyes "pulled" or turned to the right. What probably happened was that his attempt to fixate on an object produced a fluctuation, later obscuration and sometimes extinction of the image arising from his left field of vision, which was defective.

This resulted in a conflict between the right and the left side of the visuomotor mechanism. The stimuli arising from his right, or normal, field were stronger and reflexly tended to pull his eyes to the right. As the eyes deviated to the right, the regarded stationary object loomed in the left, or defective, field of vision. Of course, when the gaze to the right became extreme and the original stationary object was out of focus, or he no longer saw it, the polyopia disappeared. Also, when he turned his eyes sufficiently to the left so that the object appeared in the right or normal field of vision, the illusion was not present. From these facts it is evident that the multiple images tended to form at the transition between the defective and the normal field of vision and were related to the disturbances produced by attempted fixation, namely, obscuration and extinction of image in his left field of vision. There seemed to be a conflict between fixation and visual performance, as pointed out by Höff and Pötzl.⁸ The transient episode of visual disorientation in space was probably also related to this conflict in function.

Another form of optical illusion of cerebral origin associated with disturbances brought on by fixation is illustrated by the following case.

CASE 3.—J. E. D., a 60 year old veteran of World War I, was admitted to the hospital with a history of progressive weakness and numbness on the left side of the body, especially in the leg, for eight months. He also complained of inability to recognize and of dropping objects with his left hand. He denied having symptoms of visual dysfunction.

Neurologic Examination.—Reflex changes and motor and sensory defects were present on the left side of his body. There were mild hemiparesis and a positive Babinski sign. The sensations impaired on that side were pain, temperature, point localization, two point discrimination, position sense of digits and toes in space, stereognosis and graphesthesia. The sensory adaptation time was much reduced on the left side. All these sensations became totally extinct with the method of double simultaneous stimulation.²¹ Thus, although he could partly perceive a painful stimulus when applied to any one part of the left side of his body (distal portions were most affected), this sensation was not present when another stimulus was applied simultaneously to the corresponding part on the right side. This was true not only for pain sensibilities but for other modalities, especially graphesthesia. Even the crude sensation evoked by rubbing became extinct when both sides (hands) were rubbed simultaneously.

Psychiatric Examination.—Special psychological examinations, including the object-sorting test as devised by Goldstein and Scheerer,²² revealed abnormal rigidity of

thinking. Abstract reasoning was very poor. In grouping and sorting objects, even when prodded, he persisted in the same mental set. He arranged materials according to their everyday use. There was resistance to all the examiner's suggestions to shift to different principles of sorting. He had a tendency to be satisfied with a simple pairing of objects, and he insisted on continual manipulation of those objects which he grouped. There was extreme concreteness in his thought processes. In general, he was cooperative and persistent in his efforts. His responses appeared to be reliable and consistent.

He manifested no other signs of intellectual deterioration. His memory was good. Aside from being somewhat facetious and slightly erphoric, there was no gross disturbance of the affect. Orientation and insight were normal, but judgment was somewhat defective.

Physical Examination.—He had signs of generalized arteriosclerosis to a degree consistent with his age.²³

Ocular Examination.—The pupils were equal and reacted well to light and in accommodation. The fundi revealed retinal arteriosclerosis and normal optic disks. The ocular movements appeared to be normal and showed no apparent muscular palsy. However, during fixation it was frequently noted that the head was tilted reflexly, or without his awareness, so as to bring the object regarded into his right field of vision. The cornea, lens, other ocular media, retina and macula of

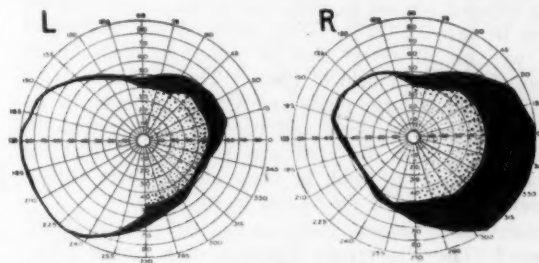


Fig. 5 (case 3).—Visual fields plotted on the perimeter, illustrating concentric form of the left homonymous field defects. With double stimulation, even perception of motion became extinct in the remaining left field of vision.

each eye were normal. He had mild astigmatism, which could be corrected.

Visual Fields and Extinction Phenomena.—Gross examination of the visual fields disclosed a left homonymous field defect, but this was not absolute (fig. 5). He could perceive motion in the left homonymous fields, but with simultaneous stimulation in the right and left temporal fields of vision, he perceived the image only in the right field; the image in the left field became extinct. The same extinction phenomenon was present on fixation of stationary objects. He had difficulty in differentiating certain hues, especially dark-toned colors.

Tachistoscopic Examination.—Exposure of images for one-tenth second under dark-adapted conditions disclosed weakness of perception in his left field of vision. With

21. Bender, M. B.: Extinction and Precipitation of Cutaneous Sensory Phenomena Illustrating Bilateral Functional Relationship of Sensation, Arch. Neurol. & Psychiat. 54:1-9 (July) 1945.

22. Goldstein, K., and Scheerer, M.: Abstract and Concrete Behavior: An Experimental Study with Special Tests, Psychol. Monogr. 53:1-151, 1941.

23. The patient offered a diagnostic problem, which to date has not been solved. Although the clinical course was that of a slowly progressive lesion, which seemed to originate in the leg area and involve largely the visual and sensory functions of the right side of the brain, there was no conclusive evidence of the presence of a space-occupying lesion. The pneumoencephalogram and the ventriculogram were considered to be essentially normal.

longer exposures, the images on his left became totally extinct. He showed normal ability to recognize images in his right field of vision when the objects were flashed at a speed of one-tenth second.

After-Imagery.—Repeated visual stimulation with strong light in either eye for fifteen or twenty-five second periods produced only a slight visual after-image, such as a "gray smudge," which lasted a few seconds. There were no color changes, as noted with the normal subject, who experiences a series of changes through yellow, blue, green, red, etc., even with as short a stimulus as three seconds. Gazing at the American flag for fifty seconds produced no visual after-image. However, after staring at the flag for fifty-five or sixty seconds, the patient saw an after-image of several brown stripes in his right upper field of vision. Besides these two vague responses, no visual after-images could be elicited with strong or weak, short or prolonged visual stimulations.²⁴ Neither positive nor negative after-images could be evoked from exposures to black or white objects under dark-adapted or light-adapted conditions. The fluctuation normally found on gazing at the Schröder staircase could not be elicited in this patient. However, he reported a fluctuating rhythm between green and red when a green lens was before his left eye and a red lens before his right eye.

Visual Retention.—The patient was confronted with a set of cards showing simple geometric figures. Each was exposed for ten seconds, and he was asked to draw what he saw.²⁵ Of the seven cards shown to him, he did well on all except that he tended to omit objects exposed in his left field of vision. Thus, when shown a small square, a large circle and a large triangle, he invariably drew the circle and triangle and omitted the square, but when the card was reversed, so that the square was on his right, he drew all the three objects presented or omitted the figures on his left side.

Monocular Diplopia, Polyopia and Other Optic Illusions.—I. The Illusion on Fixation of a Single Line: When the patient was shown lines or figures and asked to draw what he saw, he did so rather promptly, and all of his recorded images were correct and single. However, after he focused on a line for ten or more seconds, there appeared a second line parallel to the one he was regarding, and he saw two lines, one dark and one light (fig. 6 D-G). The latency varied between seven and thirty-five seconds. He saw two images with either one or both eyes and irrespective of the meridian in which the fixated line was situated. During fixation he invariably tilted and turned his head so as to bring the observed line into his right field of vision. Movements of the head produced movement of the light line. He felt that the heavy line was more or less stationary. It was difficult for him to decide in which direction the line was

24. Two months later this patient showed improvement. The monocular diplopia became less pronounced, and his ability to see visual after-images partially returned. On reexamination, he reported, after fifty seconds' exposure, a rectangular after-image of the American flag (drawn in complementary colors). Again, he saw dark brown stripes and part of the left corner field. He was characteristically unable to specify the color of spaces between these dark brown stripes, but after some reflection he concluded that they must have been "light gray." The seemingly pedantic nature of the patient's color descriptions is evidently related to his concrete mental approach.²²

25. Benton, A. L.: A Visual Retention Test for Clinical Use, *Arch. Neurol. & Psychiat.* 54:212 (Sept.) 1945.

moving relative to his head, but in general it seemed to him that the movements were to the opposite side. The monocular or binocular diplopia appeared only when he regarded thin lines. A thick line seldom produced the illusion of double image, although it tended to widen and on one occasion split in two. Actually, he never saw the splitting or the movement by which the second image appeared. On looking at a fountain pen for fifteen sec-

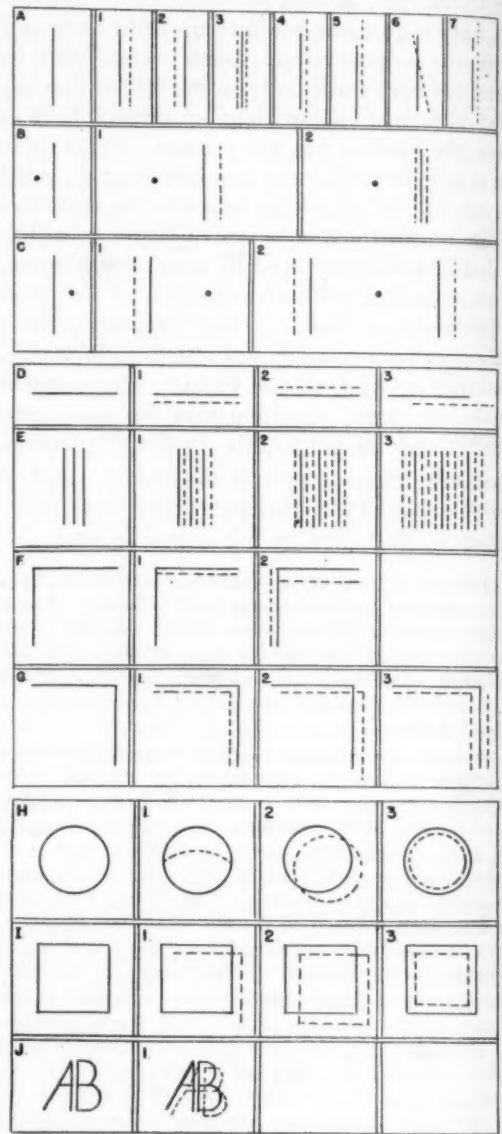


Fig. 6 (case 3).—Chart illustrating what the patient saw when presented with an object before one eye. In the first column is the drawing of the figure which was shown to him; in the columns to the right are the drawings of what he saw. The solid line represents the heavy image, while the line of dashes indicates the light image. For interpretation of these drawings, see the text.

onds, he noticed that it broadened and appeared distorted. The thinner the line, the clearer was the diplopia. Usually the images were 1/16 or 1/8 and 1/4 inch (1.6 or 3.2 and 6.4 mm.) apart when the eye was at

a distance of 10 to 12 inches (25 to 30 cm.) from the fixation point. Occasionally, he found the lighter image to be longer than the dark one. In attempts to differentiate the true from the false image, it was found that the dark, as well as the light, line was displaced from the original. The following experiments reveal some of the conditions under which the monocular diplopia could be elicited.

1. Monocular diplopia was found with either or both eyes when he was fixating on a line.

The patient was asked to fix on a thin vertical line. After the usual latency a double image appeared. When asked to indicate each of the lines he perceived, he pointed to two lines, one situated to the left and one to the right of the originally fixated line (fig. 6 A 1 or 2). He was not aware of the original line.

2. The double image appeared to be displaced.

When asked to fix at a point situated $\frac{1}{4}$ inch to the left of a vertical line, he saw after some delay two lines. When asked to put a pencil mark on each line, he pointed about $\frac{3}{4}$ to 1 inch (1.9 to 2.5 cm.) to the right of the original line, which, again, he did not see (fig. 6 B 1). At this moment, when asked to show the position of the dot, he at first localized it slightly to the right of the original, but then he corrected himself. He also had difficulty in finding the original vertical line, and when he did so the two illusory lines disappeared.

3. Double images appeared to each side of a fixated point.

When he was asked to fix on a dot situated $\frac{1}{4}$ inch to the right of a vertical line, the chin turned slightly to the left while the head and eyes rotated slightly to the right. As he executed these movements, and after a latency of three seconds, he saw two lines on his left (fig. 6 C 1) and in three more seconds another two lines, so that he saw a total of four lines, one pair about 1 inch to the left and another pair 1 inch to the right of the fixated dot (fig. 6 C 2).

4. The diplopia appeared even while the original image was moved from one side to the other of a fixated point.

The patient was asked to fix on the point of a thin stick which was placed over a piece of paper on which there was a vertical line. As he focused on the point, the paper with the line was moved laterally, and within five to ten seconds the vertical line became double. The image remained double even when the line was moved to the left or to the right, or first from right to left across the fixation point. The diplopia persisted even while the paper with the vertical line was being rotated 90 to 180 degrees.

5. The patient had formation of double images when the fixation point and the vertical line were separated by a visual angle of 2 degrees.

The patient was asked to maintain his gaze on a moving point while the exposed line remained still. Again, the image appeared double after the usual latency. In this experiment, the original image was kept stationary while the fixation point was moved to the right or to the left of the exposed line. No difference in the diplopia was elicited by this method when the object was exposed to the right and to the left of the fixation point, as in experiment 4.

6. Monocular diplopia was present for lines in the horizontal meridian.

Experiments 4 and 5 were repeated with the object a horizontal line and the fixation point changed absolutely or relatively along the vertical meridian. The same results were obtained (fig. 6 D). The diplopia was found to be present over a radius of $\frac{3}{4}$ inch from the fixation point, or a visual angle of 2 degrees.

7. The double or multiple images were present within a definite range along the visual axis.

Thus, the exposed object appeared (a) blurred when situated less than 15 cm., (b) clear but double when situated between 15 and 63 cm. and (c) clear and single when situated more than 63 cm., from the eye. The diplopia and polyopia were most pronounced when the exposed line was set between 25 and 40 cm. from the cornea.

8. The partial or complete covering of the exposed object produced a concomitant disappearance of the illusory images.

Experiment 2 was repeated. When the image appeared to be double and displaced about $\frac{3}{4}$ inch lateral to the position of the regarded object, a piece of paper was placed on the original line. This immediately caused disappearance of the induced double images. As soon as the paper was removed and the line was reexposed, the patient again saw the two lines. Covering only a part of the line resulted in the eclipse of that part of the double image.

These observations seem to indicate that the images the patient had of a fixated line were false, despite the fact that one of them was dark and the other light. One may claim that the dark line is a displaced true image. This, however, is invalidated by the observation made in experiment 3. There the patient saw a dark and a light line to the left and a similar pair to the right, of a fixated point. Thus, in a field where only one line was exposed $\frac{1}{4}$ inch to the left of a focused dot, the patient saw two dark and two light lines (fig. 6 C 2).

II. Polyopia and the Illusion Found on Fixation of More than One Line: When the patient looked at two or three parallel lines, he saw six, at times nine and once twelve, lines (fig. 6 E 1 to 3). Thus, the patient had not only monocular diplopia but polyopia (see also fig. 6 A 3 and B 2). The polyopic images were parallel, and most of them were lighter than the original. When asked to count the heavy lines, he pointed out three of them, but at times he thought he saw more. Because of the great number of lines, he became confused when he attempted to count them. He found it difficult to determine on which side the lighter images appeared. Usually, however, he located them to the right. Thus, while studying the position of the six images, he discovered three more on slight turn of his head to the left, and with another slight turn he saw three more, forming a total of twelve (fig. 6 E 3).

Focusing on lines drawn in two planes was also accompanied by monocular or binocular diplopia, after a latency of eight to fifteen seconds. The entire image appeared double. However, if the greater part of the exposed figure was in the patient's right field of vision, he saw double only for the part exposed in his right field (fig. 6 F). This was inconstant and depended on the point of fixation.

III. Illusions Produced by Curved Lines, Geometric Figures and Other Mixed Lines: When asked to draw what he saw on fixating on a circle, he gave three types of responses: a circle, with a lighter arc drawn within it; two circles, one linked above with the other, and or a circle within a circle (fig. 6 H). On looking at a square, he saw double after a given latency (fig. 6 I). At times the double image was incomplete (fig. 6 I 1 and H 6). When he was asked to draw the letters A and B after he had fixated on them, he drew a double image of each (fig. 6 I).

IV. Other Illusions: On occasions he noted a discontinuity in the dark and light lines of the double image, usually in the upper part of the field of vision. The patient volunteered that the lines, circles or geomet-

ric figures had "gaps" in their upper portions (fig. 6A7).

In general, most of the illusionary figures were parallel, but on one or two occasions there was a tilt of one of the two images seen on fixating on a single straight line (fig. 6A6). On several occasions, it was found that one vertical line was slightly lower than the other (fig. 6A5) or one horizontal line was farther to the left or to the right than the other (fig. 6D3) or one was somewhat longer than the other (fig. 6A4).

As stated before, the latency varied. However, once the patient had monocular diplopia or polyopia, he was able to see as double all other objects submitted to him within a very short latent period of one to three seconds. When the eyes were rested, by closing the lids for more than fifteen seconds, and the tests were then resumed, the latency for the monocular diplopia was again prolonged to ten or twenty-five seconds. If the rest was less than ten seconds, the latency remained short, i. e., one to three seconds. The patient had no difficulty in reading as long as he did not stop to look at one spot for any length of time.

Comment.—This case demonstrated several interesting phenomena: (1) extinction of visual, as well as of cutaneous, sensations on the left when the right and the left side were stimulated simultaneously; (2) defective visual after-imagery; (3) impairment of the mechanism of fixation and (4) monocular diplopia, polyopia and other optic illusions on attempted fixation.

It is significant (a) that the multiple images in this case did not occur unless the objects studied were represented by thin lines, (b) that they did not appear unless the object was fixated over a latent period, which sometimes lasted thirty-five seconds, and (c) that the illusion was present only in a given zone of the projected field of vision. Also important were the association of the diplopia with observable deviation of the eyes and the displacement of all the images. This displacement took place usually to the right, but in many instances also to the left. However, the change in the position of the images occurred even without deviation of the eyes (experiments 4 and 5).

It was not always related to the position of the eyes; thus, the patient saw double while the exposed object was rotated slowly through 180 degrees. If it was rotated rapidly, the diplopia disappeared. Still another important observation was that the illusion appeared only within a certain range—within 2 to 3 degrees of the fixation point and between 15 and 65 cm. from the cornea. Beyond these limits there was no monocular diplopia or polyopia. Evidently, the illusions depended on fixation and seemed to be related to the conflict between the right and the left field of vision.

CASE 4.—J. P. F., a 20 year old seaman, second class, was admitted to the hospital with a temperature of 106 F. He had a maculopapulomorbiform eruption over the face and trunk, Koplik's spots, pharyngitis and con-

junctivitis. The diagnosis was measles. For the first six days the temperature ranged from 101 to 105 F. He was treated with penicillin and apparently improved. Fifteen days after the onset of the illness, his temperature again rose to 102 F., and he became restless and suffered from insomnia. He had diarrhea, urinary retention and defective vision, and there developed typical signs of paralysis agitans. There were bradykinesia; forward bending of the trunk; abduction of the arms with loss of associated arm and finger movements; pill-rolling tremor of the fingers, especially on the right; increased muscular tone; fixed and greasy facies, and infrequent blinking. There was a congenital convergent squint in the left eye. In addition, he had many visual disturbances, which will be described in detail later. On psychiatric examination, he was found to be euphoric, facetious and impulsive. At times he showed involuntary laughter. Memory was defective, and calculation was poor. There was severe insomnia, and one night he had visual hallucinations. He also showed compulsive and obsessive phenomena. He was unable to adjust to the temperature of the room. He often complained that it was cold when actually the temperature was above 80 F., and vice versa. For several days he had urinary retention, and once he was incontinent. Except for leukocytosis, all laboratory studies, including those of the spinal fluid, revealed nothing abnormal.

By the fifth week of his illness he was much improved. The mental symptoms had subsided; the tremor and other signs of paralysis agitans were minimal. The arm swing returned, and the facies became more expressive. However, he still complained of defective vision (that objects were obscure) and of inability to read quickly or to see individual units. He had illusions of seeing groups of objects which seemed to be displaced in space. Some of these visual symptoms persisted for several weeks. The plotted visual fields failed to disclose any gross scotomas or contraction. Visual acuity was 10/40 in the right eye and 10/50 in the left eye. During his convalescent period, he was observed frequently, and numerous studies revealed pronounced defects in the visual perceptive mechanisms.

In the first few weeks of his illness, he showed marked defects in perception, as tested with the tachistoscope. Even with one second exposures, he was unable to detect simple objects, letters, geometric figures or colors. But with longer exposures he could identify each of the objects presented.

His drawings were extremely poor. They showed marked disproportion of the figures and ground and omission of essential lines, contours and shadows. He knew a hexagon had six sides, but he drew only five. On drawing a checkerboard, he failed to differentiate black and white squares. Visual retention was defective, inasmuch as he omitted details.²⁶ Dark adaptation time was nine and one-half minutes on the Feldman adaptometer.

Visual after-imagery had disappeared almost completely.²⁶ The only visual after-image which could be elicited in this patient was that induced by shining a strong light in either eye. After a five second stimulus, he saw in the dark, or with his eyes closed, a small round white light, which persisted for over eight minutes without changing its color.²⁷

26. The patient stated that prior to his illness he was able to see negative after-images with black, white and various color stimuli.

27. In the normal subject such a stimulus produces a visual after-image of a white-yellow light, which changes to blue, to green, to red, and ultimately to black and tends to disappear entirely within two to three minutes.

for the first
to 105 F.
y improved.
his tempera-
restless and
inary reten-
typical
adykinesia;
e arms with
pill-rolling
; increased
infrequent
squin in
visual distur-
later. On
e euphoric,
involuntary
ulation was
ight he had
pulsive and
just to the
ined that it
above 80 F.
inary reten-
or leukocy-
of the spinal

h improved.
tremor and
l. The arm
expressive.
vision (that
d quickly or
of seeing
ed in space.
for several
disclose any
was 10/40
During his
uently, and
ects in the

ved marked
chistoscope.
unable to
s or colors.
each of the

ey showed
ground and
adows. He
ly five. On
ntiate black
ffective, in-
tation time
n adaptom-

most com-
h could be
shining a
d stimulus,
ed, a small
over eight

ess he was
white and

roduces a
ich changes
black and
minutes.

He complained of inability to read as quickly as he could prior to his illness. He had to follow the print slowly or he would skip words. He could not recognize simple words when they were inverted or turned 90 degrees to the horizontal. When he looked at a picture magazine, he could not appreciate what he saw at a glance. It was necessary to study individual parts "to see the picture or to get its meaning."

About this time, special tests revealed defectiveness in visual organization which approached genuine visual agnosia. On attempting the "performance scales" of the Bellevue-Wechsler intelligence test, the patient was unable to visualize the "hand" which had to be assembled from seven irregularly shaped pieces of wood. After ending his performance with an absurd configuration, he indicated to the examiner that he was aware of his failure.

Color vision at this time appeared to be normal, but he had great difficulty in recognizing the figures exposed in color tests, especially on the tachistoscope.

During the sixth week of his illness, he noticed small yellow "spots and bands" whenever he regarded an object or print. These spots moved with his eyes and were present even when his eyes were closed.

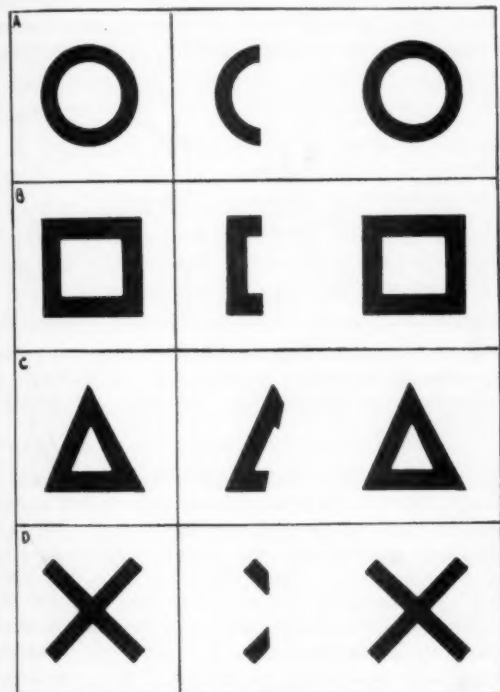


Fig. 7 (case 4).—Chart illustrating what the patient saw when he looked at simple geometric figures. In the first column is the figure shown to the patient, and in columns to the right are the drawings of what the patient perceived.

During the seventh week of his illness, some of his ability to see after-images had returned. When the American flag in complementary colors of some other colored object was exposed, he saw a small gray after-image of the exposed object. He saw the background or outline but not the figure. The following week he noticed the figure, but it was gray. Thus, he saw gray and white stripes instead of the red and white stripes of the American flag. Negative after-imagery in

complementary colors did not return until several weeks later, and then it could be elicited only after prolonged stimulation. The patient could see negative after-images of thick black lines. When he discovered that he had regained part of his power of visual after-imagery, he rejoiced and repeatedly tested himself by exposing his eyes to all sorts of black lines and figures. However, after a few days of such experimenting, the patient began to see double. He complained that on looking at black objects he saw another partial image to the left of the original. This was present when he used both eyes or when he closed the left eye. At first he

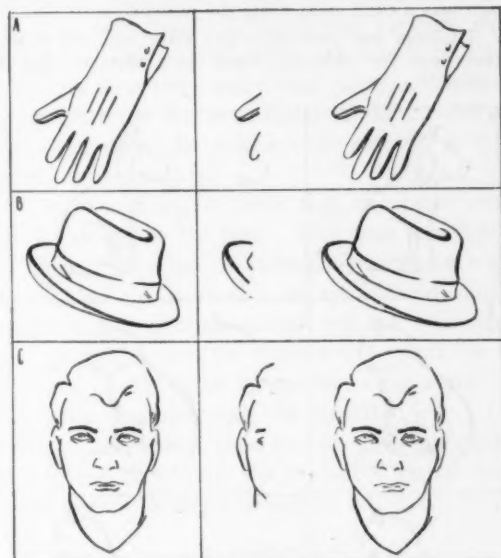


Fig. 8 (case 4).—Examples of what the patient saw (monocular diplopia) when he looked at symmetric objects and the face with his right eye. Columns are arranged as in figure 7.

thought it was an after-image, but he soon found that he could see the negative after-image in white, in addition to the black double image on the left. At times the negative after-image was on the right, but the second positive image, which was partial, was always on his left. For this reason, a battery of tests was given, and the observations which follow were made on testing the right eye; satisfactory studies could not be carried out on the left eye because here vision was poor.

1. The second, or false, image was always to the left and represented the extreme left portion of the original ground and figure exposed (fig. 7). It was always incomplete. At times the second image was situated on a slightly lower plane than the original image. The latency for the appearance of the second image was less than one second.

2. The diplopia was present for all types of objects he regarded: lines, geometric figures and drawings, faces, etc. (figs. 7, 8, 9 and 10).

3. The false, or partial, image always appeared fainter than the original image, even though it retained the color, contour and size of the left side of the original object exposed. The patient described the distinctness of the false image as being similar to that of the image which he perceived with the squinted eye. The right edge of the false image was never sharply demarcated and seemed to merge with the background.

4. The incomplete second image was seen even while the object was in motion (horizontal, vertical or circular motion). The false image of the object in motion was always incomplete and represented whatever there was on the left side of the original.

5. The monocular diplopia was present when the object was situated up to within 3 degrees of the fixation point. Beyond this visual angle, there was no diplopia except that for the fixation point itself.

6. The original and the partial image on the left generally kept their relationship in space as the object was moved from one point to another in the field of vision. The double images separated only when the original image was moved away from the patient.

7. Diplopia was present in any direction, and to some extent even for objects viewed at a distance, but the

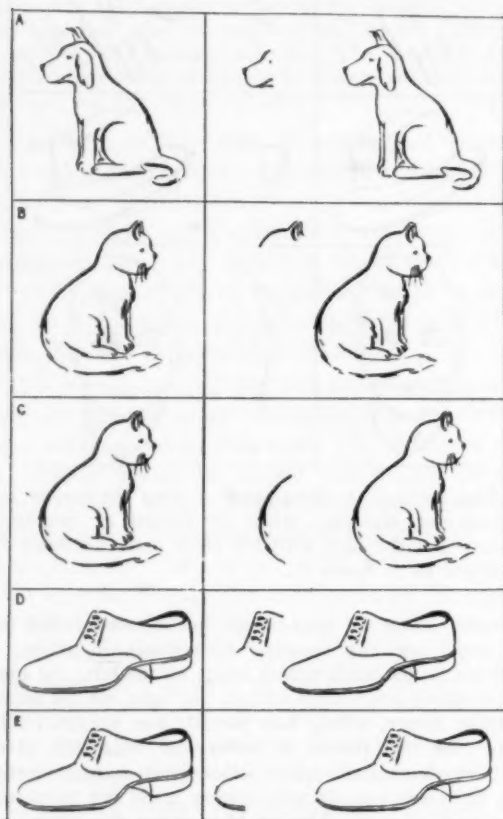


Fig. 9 (case 4).—Examples of what the patient saw (monocular diplopia) when he looked at asymmetric objects with his right eye. Columns are arranged as in figure 7.

greatest amount of diplopia was for objects at a near point. The nearer the object was held to the patient, the more of the false image was visualized.

8. When the original object was covered, the false image disappeared. At times the patient perceived both the negative visual after-images and the incomplete false image after prolonged fixation on the object; covering the original object abolished the false image but not the after-image.

9. When the patient regarded objects which were asymmetric in their contour, he saw different types of false images, depending on on which part of the object he fixed his vision. Thus, on looking at the dog in figure

9 A, he saw part of the snout to the left of the original. When he looked at the cat (fig. 9 B), he saw the ears and part of the head to the left. However, when he was asked to gaze at the middle of the cat, he saw the back in the false image (fig. 9 C). The same was true when he looked at the shoe (fig. 9 D and E). In other words, the center of attention of the figure and ground attracted the patient's eyes, and this fixation point determined what part of the original object appeared in the false image.

10. On studying the Schröder staircase effect, the patient saw the extreme left part of the staircase to the left of the original. He found that the staircase fluctuated in its position and that the false image fluctuated *pari passu* with the original. When the picture looked like a staircase, he saw an additional step to the left of the original (fig. 10 A). When the stairs appeared inverted, like a cornice, he could not see the outline of the false image, although he felt something was there; the stair in the false image disappeared, and there was only a corner (fig. 10 B). When the stairs flipped back to the upright, or original, position, he saw the extreme left step in the false image.²⁸

11. In order to analyze further the role of fixation and of ocular movements during fixation in this patient's monocular diplopia, the following experiments were performed: The patient's ocular movements were observed by three different methods (pinhole, mirror and after-

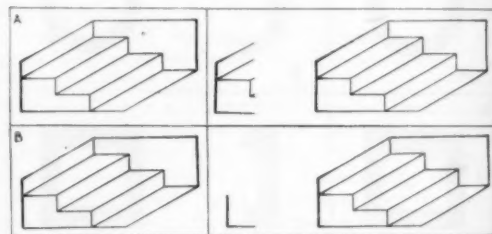


Fig. 10 (case 4).—Types of double images the patient saw when he looked at an object which fluctuated in its figure-ground relationship. Columns are arranged as in figure 7.

image). All these studies revealed that the diplopia in the right eye occurred concurrently with lateral nystagmoid excursions of the globe during fixation. This was particularly evident with the method of after-imagery. The after-image of a small white luminous disk (produced by stimulating the patient's right eye with the ophthalmoscope) traveled horizontally to the left, starting slightly above the center of a red cross which the patient was instructed to fixate. These excursions repeated themselves until the after-image faded away. It was during these experiments that the patient discovered to his surprise that the excursion of the after-image (and the implied shift in fixation) invariably came to a halt vertically above the incomplete double image of the cross. This double, or false, image appeared as usual to the patient's left and slightly below the

28. The patient thus gave a striking illustration of one of the main tenets of the Gestalt theory of perception, namely, that figure and ground are of necessity inseparable in percept formation (Köhler, W.: *Dynamics in Psychology*, New York, Liveright Publishing Corporation, 1940. Koffka, K.: *Principles of Gestalt Psychology*, New York, Harcourt, Brace and Company, Inc., 1935).

original. It always remained stationary and never shifted about, like the after-image.²⁹

After one week the monocular diplopia diminished. It disappeared altogether in the left eye. (In this eye the diplopia was found only the first day and could be elicited with difficulty and never clearly.) At this time, the diplopia was found in the right eye only when the patient fixated with the globe or held the head in a certain position. With both eyes the patient continued to see double, but the pattern of the images was the same as that noted in the diplopia seen with the right eye. During the tenth week of his illness even the binocular diplopia had begun to disappear. However, when the right eye was tested repeatedly over a period of several hours, the monocular diplopia in this eye again became very apparent, and he was troubled with it for several days thereafter. The patient disliked being tested, as he feared recurrence of the diplopia.

Comment.—This patient had encephalitis following measles with clinical signs of involvement of the basal ganglia, hypothalamus, occipital lobes and probably many other parts of the brain. The syndrome of paralysis agitans and mental and other symptoms disappeared within a short period, but the visual troubles were most profound and lingered for some time. He showed disturbances in his visual Gestalt and after-imagery.

It is significant that the monocular diplopia (an original and an incomplete false image) appeared at about the same time that his ability to see after-images had returned. It is also significant that this patient had convergent strabismus. Since it is known that monocular diplopia may be induced in persons with squint, the question arises whether the patient did not induce a diplopia in himself by sensitizing the already diseased occipital lobe when he studied the negative after-images so avidly during the seventh week of his illness.³⁰ That such diplopia may have been induced in this case is suggested by the observation that repeated visual stimulation for tests of diplopia produced a recurrence of the symptoms during his period of recovery.

Another factor to consider is that of the spots about which the patient complained whenever he attempted to read or to regard an object. These spots were constantly present in his central field of vision and tended to interfere with his power of fixation. It is possible, therefore, that this disturbance in fixation was partly responsible

for the monocular diplopia, especially since he already had a false macula in the left eye and thus probably an additional set of "space values" in the cortex.

The most unusual feature of all, however, was the incompleteness of the false image. The second image seemed to be a duplicate of the extreme left portion of the original, as though the original were covering all but the extreme left portion of the false image. This incompleteness of the false image may have been the reflection of a disturbance in his visual Gestalt, since the patient was unable to see the whole of a picture. He saw only individual parts. Whatever the mechanism for monocular diplopia may be, this is one example in which the second, or false, image is incomplete.

It is interesting to note that the false image was localized to the left. This was the side of his body and of his surroundings in space which represented poor vision, as symbolized by the amblyopia ex anopsia in the left, or strabismic, eye. Furthermore, the patient described the appearance of the false image as being similar to that which he had with the squinted eye. It is possible, therefore, that the second, or partial, false image represents the projected visual image of the psychologically defective left eye.

COMMENT

The first 3 cases described in this report show several things in common, namely, (a) scotomas in the fields of vision; (b) fluctuation, obscuration or extinction phenomena in the defective fields of vision; (c) disturbance in the mechanism of fixation, and (d) optical illusions. The fourth case is somewhat different, inasmuch as there were no demonstrable field defects and the double, or false, image was incomplete. Naturally, the first impulse is to attribute all these symptoms to a common cause, but this is possible only from the structural standpoint.

One may safely assume that the scotomas were produced simply by damage to the calcarine cortex or the optic radiation. Here destruction of tissue produced absence of function. The rest of the symptoms, however, cannot be explained on a structural basis alone. They seem to be an expression of normal functions which become apparent only under pathologic conditions. Thus, in a previous communication, it was pointed out that fluctuation, obscuration and extinction of visual perception are psychologic phenomena which become evident in patients with diseases of the visual cortex or pathways.¹⁵ This apparent disorder in perception is due to the presence, and not to a lack, of function.

29. Owing to the importance of these observations, the detailed discussion of them and of the methods employed will be given in a separate report. The after-image method for observation of ocular movements was used extensively by Helmholtz and other earlier physiologists (von Helmholtz H.: *Handbuch der physiologischen Optik*, Leipzig, L. Voss, 1911).

30. Tschermak, in 1899, and Sverdllick, in 1938, both of whom were cited by Cass,⁴ considered the relationship between monocular diplopia and visual after-images.

Disturbances in the mechanism of fixation, as noted in the cases described here, are also expressions of underlying normal functions which are thrown out of equilibrium.

Fixation is maintained by a constant muscular effort in which the actions of all the ocular muscles are balanced. This constant activity results in fine rotatory movements, in which, although the globes may seem to be at rest, they are never completely immobile. According to Duke-Elder,³¹ three types of movements are evident in the act of fixation; (a) relatively large, jerky excursions through an average angle of 4 minutes or more, recurring at intervals of from one to two and one-half seconds; (b) in the interval between these, when the eye appears at rest (the period of elementary fixation), a constant succession of much more rapid, fine, "twittering" excursions, through an angle of 1 minute, with a duration of one to two and one-half seconds, and (c) superimposed on these, a minute variation in the position of the head. As a consequence of these movements, the region of the retina which is used in fixation, i. e., the fovea, occupies a considerable area. These movements occur equally in each eye, whether used for near or distant vision or whether one or both eyes are employed in fixation. These movements vary considerably with each subject, with the state of adaptation of the eye and with illumination. Such constant movement, although not apparent, is important in the physiology of vision and is pertinent to the discussion of monocular diplopia and polyopia.

It is probable that the continual movement of the globe during fixation leads to stimulation of more than one retinal point in the fovea. If there happens to be a disturbance in the mechanism of fixation, the movements of the eyes are more pronounced, and slight ocular deviations may become grossly apparent.

Now, one of the chief causes of disturbance in the mechanism of ocular fixation is disease of the occipital lobe. The occipital lobes are largely responsible for initiating movements in the eyes which bring them into a position of fixation. When one of the lobes is defunct or loses its influence on the position of the eyes, the normal occipital cortex is unopposed in its function, and there results an imbalance between the opposing forces. During the act of fixation, impulses reach the normal side and tend to pull the eyes in that direction without opposition from its antagonistic, but diseased, side. If the deviation is slight, the patient is unaware of it, even though the retinal image falls on a new fovea.

31. Duke-Elder, W. S.: *Text Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, p. 589.

Another cause of defective fixation is the phenomenon of visual extinction. When an image from a defective field of vision fluctuates in its appearance, or becomes obscure, or even extinct, as a result of competition between the healthy and the diseased side of the brain, the associated reflex visuomotor reactions come into operation, with resultant domination in motor function by the normal side. This imbalance in motor influence produces a tonic deviation of the head and eyes, and, because the image cannot fall on the true macula, there is further difficulty in fixation. Whatever the cause of dysfunction in the mechanism of fixation may be, the reflex and unconscious ocular deviation will cause the image of the regarded object to fall on a retinal point other than the true macula and thus form a new, or false, macula. If this new point is near the true macula and the constant and rapid ocular movements which occur during the act of fixation are such that both the true and the false macula are stimulated within a fraction of a second of each other, there results a conflict between the visual sensations thus evoked at the two retinal points. Such a conflict will result in defective vision, in the formation of more than one image, or in normal vision if the true macula dominates over the false. This leads to the discussion of the fourth common symptom in the group of cases herein reported, namely, monocular diplopia and polyopia. In an attempt to explain these optical illusions it is necessary to consider the physiologic and psychologic components of the fields of vision.

The ability to localize the position of an object in space depends not only on vision but on tactile, postural and labyrinthine sensations. All of these body sensibilities are integrated into a scheme which is represented in the brain, and this, in turn, is oriented in relation to the scheme of the external world. Visual localization is a process which involves (1) a relative factor, or localization of an object relative to the fixation point, and (2) an absolute factor, or localization of the fixation point with reference to the observer. The position of each stimulated visual point acts on the "mind,"³² and the relation of all the visual localization points is maintained in the cortex. The fovea forms the primary point of reference, and the images formed thereon are projected on a line which passes outward through the nodal point of the eye, or the fixation line. About this point of reference the field of vision is so spatially organized that the person is aware of a "right," "left," "up" and "down" and

32. Sherrington, C.: *The Proprioceptive Function of the Extrinsic Ocular Muscles*, *Brain* 41:332-343, 1918.

the center, which is "straight forward" or "just before me." The center of the field determines the subjective median point. In the normal person, the latter coincides with the objective median zone, or the macular region. This entire scheme of the perceptive field of vision is also projected on the occipital cortex.

In patients with squint or with scotoma involving the macula, the subjective median plane is displaced, and there is no longer correspondence between it and the objective median zone. When there is weakness of the eye muscle or faulty fixation, either of which produces slight ocular deviation, the image of the regarded object is projected on a new macula. This, in turn, leads to a reorganization of the perceptive field of vision about the new macula. The functional values of points in the retina change and rearrange themselves in relation to the new macula, thus forming a new center of distinctness. In other words, the patient learns to use a new fovea. The location of the new fovea is not fixed and may not be far away from the old, or congenital, fovea. The distance between the anatomic and the functional fovea is determined largely by the Gestalt of the object.³³

With the establishment of a new macula and its consequent reorganization of the field of vision, there occurs a corresponding change in the occipital cortex. Stimulation of the new macula leads to perception of an object, just as stimulation of the old macula did.

If both maculas are stimulated simultaneously, diplopia results. In cases of congenital squint the images obtained from the squinted eye are psychologically suppressed, and there is no binocular vision. But if the true and the false maculas of the squinted eye are stimulated simultaneously, as demonstrated by Cass, monocular diplopia will appear. In cases in which there is faulty fixation, and therefore more than one functional macula, the rapid movement of the eyes during the act of fixation might produce the effect of simultaneous stimulation of the true and the false macula, with resultant monocular diplopia. The same analogy holds for polyopia, in which several new functional maculas have been established in the cortex.

That monocular diplopia and polyopia are largely due to development of new maculas and faulty fixation is well illustrated in cases 3 and 4. In case 3, the illusion was present only within 2 degrees of the median point, when the exposed

object was situated within 63 cm. of the projected line of fixation, and it did not appear unless the patient attempted to focus on the object. Furthermore, he had difficulty in maintaining his gaze, since there was a conflict between the right (normal) and the left (pathologic) field of vision.

In case 4, the monocular diplopia was also limited to the foveal area. On several occasions the patient had to turn his head and eyes and focus on the object in a certain position before the diplopia appeared. Furthermore, direct observation by three different methods revealed nystagmoid movements during fixation, and it was during the movements of fixation that the monocular diplopia became apparent. Although he showed no demonstrable field defect, he had a subjective scotoma about his fixation point. He complained that the spots before his eyes (in the subjective median plane) covered part of the print and he could not see clearly. This implied that in his attempt to see "better" he tried to fix on the object in some manner, thus revealing a disturbance in fixation, and it is also probable that because of the subjective scotoma a new macula may have formed.

The patients in cases 1 and 2, although not studied while they had polyopia, gave a history, and later showed residual signs, of difficulty in fixation and visual defects, with probable formation of new maculas. In case 2, the more the patient tried to fix on an object, the more blurred and multiple it appeared. The quadruplopia, with images appearing in the vertical and horizontal meridians, as described in case 1, may have been due to the partially altitudinal and partially lateral hemianoptic field defects. It is possible that the altitudinal defect produced a reflex deviation of the eyes in the vertical plane and thus led to formation of double images in this direction, in the same manner as lateral hemianopsia produces diplopia or polyopia along the horizontal meridian.

On the basis of the observations made in the cases reported here, it is apparent that monocular diplopia and polyopia are indirectly attributable to imperfect fixation. As already pointed out, defective macular vision leads to difficulty in ability to fixate, and, conversely, imperfect fixation stimulates the formation of new maculas. In either instance, the power to maintain the eyes on a given point is impaired, and this, in turn, creates an increase in the amplitude of the ocular excursions normally present during the act of fixation. Such an increase in ocular movements will, in effect, cause different macular points in the foveal area to be stimu-

33. Fuchs, W.: Untersuchungen über das Sehen der Hemianopiker und Hemiamblyopiker: I. Verlagerungserscheinungen, *Ztschr. f. Psychol. u. Physiol. d. Sinnesorg.* **84**:67-169, 1920; II. Die totalisierende Gestaltauffassung, *ibid.* **86**:1-143, 1921.

lated repeatedly and at a rapid rate, with consequent activation of their functional centers and the corresponding space values. An analogous situation can be found in cases of cutaneous sensory disorders in which repeated stimulation of a functionally disorganized area evokes more than one sensation (synesthesia). From these considerations one may deduce the theory that it is the repeated stimulation of a functionally disorganized sensory area which "fires off," or activates, more than one functional center (and space values) at a time, thus yielding multiple images. Although this does not disprove Goldstein's contention of "diffusion of an excitation" in the cortex, it is felt that this theory adequately explains monocular diplopia and polyopia.

In general, it would seem that multiple image formation is due to a disorganization in function produced by disease of structure. Since monocular diplopia and polyopia are the result of a dynamic disequilibrium in psychologic visual

functions, it is readily understood why these symptoms are often so transient. The organism learns to correct its seeing of an abnormal number of images by selecting or finding one of the several available maculas and assigning to it all the sensory and motor attributes necessary to keep it as the dominant central point in its newly organized field of vision.

SUMMARY

Cases of objective and subjective disturbances in the visual fields with associated defects in mechanisms of fixation are described. The patients had either monocular diplopia or polyopia or both, and some of them also had symptoms of spatial disorientation. It is concluded that the rapid and involuntary movements of the eyes produced by faulty fixation tend to stimulate, simultaneously, the original macula and any new maculas which may have been formed as a result of impairment of vision.

United States Naval Hospital, San Diego, Calif.

THE HUMAN PYRAMIDAL TRACT

XIII. A STUDY OF THE PYRAMIDS IN CASES OF ACUTE AND CHRONIC VASCULAR LESIONS OF THE BRAIN

A. M. LASSEK, PH.D., M.D.

CHARLESTON, S. C.

The purpose of the present investigation is to correlate as nearly as possible the motor deficits produced in striated muscles by cerebrovascular lesions with axonal destruction in the pyramids. Such injuries, in the form of emboli, thromboses or hemorrhages, are known to have a destructive action on nerve tissue. It may be possible that these three forms of vascular disturbance do not act in exactly the same manner on the neurons of the pyramidal tract. Wide variations in the extent and potency of each type may be the rule. Although it appears that the true status of the cerebral collateral circulation has not been definitely settled, this vascular supply may be a factor in maintaining the viability of neurons under certain pathologic conditions, especially those of the thrombotic type. All of these factors may be reflected in the damage done to the axons of the pyramidal tract.

The pyramidal fasciculus is regarded as one of the most susceptible to disease processes in the central nervous system. This view has been formulated largely on the results of comparative phylogenetic and ontogenetic studies of nerve tracts, which, in turn, have been correlated with the frequency of clinical involvement of the tracts. On this basis, the pyramidal pathway should be preeminently unstable and easily destroyed, since it is the last to appear in the animal scale and, also, in the individual development of the human.

Paralysis is a common clinical symptom which has always been associated with destruction of the pyramidal tract. The question arises as to how much fiber loss is necessary to produce muscular disability. Apparently, few detailed and specific studies have been made in this respect. Supratentorial vascular lesions must always occur in the region of complex cell and fiber structures, i. e., the cerebral cortex, the internal capsule, the association bundles, the

thalamus, the corpus striatum, the substantia nigra and the claustrum. It is estimated that there are about 12,000,000,000 cells in the cerebral cortex alone, and each must give origin to an axis-cylinder, according to the neuron theory. Involvement of nonpyramidal motor and sensory fibers may, therefore, be relatively great with the majority of high vascular lesions. The pyramidal fibers may comprise but a small percentage of the total number destroyed in the majority of cerebrovascular insults.

The following characteristics make the pyramidal tract acceptable for the present problem: It is regarded as the great voluntary motor tract; it has a central origin from the cerebral cortex; it occupies a midposition in the internal capsule; it is almost completely isolated in its course through the pyramid, and it is supplied by all the vessels which course to the brain, including the lenticulostriate artery.

MATERIAL AND METHODS

The study consists in an analysis of 106 selected cases of vascular lesions obtained through the cooperation of several neuropathologic departments. The hospitals, with the number of cases contributed, are listed as follows: Montefiore Hospital, 22 cases; Philadelphia General Hospital, 19 cases; Cincinnati General Hospital, 17 cases; Barnes Hospital, St. Louis, 15 cases; Neurological Institute of New York, 14 cases; Mount Sinai Hospital, New York, 14 cases, and Well-fare Island, N. Y., 5 cases.¹

Fifty-eight patients were males; 44 were females, and the sex of 4 could not be determined. The average age was 53.3 years. In all of the 106 cases some form of motor deficit existed, with one or more of the classic signs referable to the pyramidal tract. In 55 cases a clinical diagnosis of hemiplegia was made; in 19 the clinical sign was hemiparesis, while in the remaining 32 cases the diagnosis was made under various terms such as paralysis, loss of muscular power,

1. The following physicians cooperated in making available the material for this study: Dr. C. D. Aring, of the Cincinnati General Hospital; Dr. Charles Davison, of Montefiore Hospital, New York; Dr. J. H. Globus, of Mount Sinai Hospital, New York; Dr. Helena E. Riggs, of Philadelphia General Hospital; Dr. W. O. Russell, of Barnes Hospital, St. Louis, and Dr. A. Wolf, of the Neurological Institute of New York.

From the Department of Anatomy, Medical College of the State of South Carolina.

Aided by a grant from the Committee of Scientific Investigation of the American Medical Association.

limping or weakness. In 69 cases the condition was judged to be of the chronic and in 37 of the acute type. The duration of motor symptoms varied from three days to twenty-one years, the average being two and a half years. In any case in which symptoms of muscular disability were in evidence longer than two months the disturbance was classified as chronic irrespective of other disease symptoms. Recurrent strokes occurred in some cases. In 40 cases a Babinski sign was elicited at some stage of the paralysis; in 7 cases there was a questionable Babinski sign; in 4 cases there was an Oppenheim sign; in 2 cases a Hoffmann reflex was recorded; in 3 cases the clinicians stated definitely that there was no Babinski sign present; in 1 case signs of involvement of the pyramidal tract were recorded by the observer, and, finally, in 49 cases no report was made as to the status of the pathologic toe reflexes.

The pathologic diagnoses of the cerebrovascular lesions were as follows: subarachnoid hemorrhage, emboli, thrombi, intracranial hemorrhage, softening, encephalomalacia, cystic malacia, chronic hematoma, ruptured aneurysm, venous thrombosis and hemorrhagic infarct.

Only the pyramids of the medulla oblongata were examined. The specimens were all fixed in dilute solution of formaldehyde U. S. P., and the axons were stained with Davenport's silver nitrate method in the first stage of the investigation and with Bodian's technique later. The Loyez method was employed for staining myelin sheaths in about one-half the specimens. In some cases sudan III was employed for fat. More reliance was placed on the sections stained with the silver methods.² For various reasons, no standard level of the medulla could be examined. In some instances both cross and longitudinal sections were examined, but the majority of sections were in the former group. The amount of fiber loss was merely estimated in all cases.

RESULTS

In 7 of the series of 106 cases,² complete destruction of the pyramidal tract was indicated by a study of the pyramids. In 36 other cases there were varying amounts of degeneration, ranging from slight to almost complete. In the remaining 63 cases there was no overt evidence of a degenerative process. In the last group it is possible that some fibers may have been missing or slightly altered, so that changes could not be ascertained from microscopic examination. If this were true, however, it would seem that the loss would be minimal.

The following 11 cases in the series illustrate the signs, symptoms and pathologic changes, in all of which there was no evidence of destruction of the pyramidal tract.

CASE 1.—A woman aged 58 was admitted on Nov. 2, 1939 and died November 25.

History.—Right hemiplegia with aphasia developed five years prior to her admission to the hospital. A second episode, also with aphasia, occurred two years previously.

2. Miss Iseult V. Finlay and Miss Margaret Powers carried out all phases of the technical staining procedures.

Examination.—Palsy of the right side of the face of the upper motor neuron type was observed. The tongue deviated to the right. Motor weakness of the right upper and lower extremities was present. The abdominal reflexes were absent on the right side. Hoffmann and Rossolimo signs were present on the right side. A suprapatellar clonus was elicited on the same side. There was definite motor aphasia.

Course.—The patient suffered a third vascular accident on November 23. At this time she had left hemiplegia with weakness of the left side of the face of central type. The deep reflexes were much stronger on the right side than on the left. Abdominal reflexes were not elicited. The feet were in the chronic Babinski position, and there was a marked grasp reflex on the right. The patient died two days later.

The duration of motor symptoms was five years.

Autopsy.—A large subarachnoid hemorrhage extended over part of the motor, parietal and superior temporal convolutions. A frank hemorrhage involved the white and gray matter of the superior part of the motor, the inferior parietal and the temporal convolutions.

Microscopic Diagnosis.—The diagnosis was generalized cerebral arteriosclerosis, hypertension and hemorrhage along the distribution of the right cerebral artery.

Examination of the Pyramids.—There was no observable loss of axons in the pyramidal tract.

CASE 2.—A woman, whose age was not given, was admitted to the hospital Sept. 20, 1937 and died Jan. 2, 1939.

History.—In 1934 the patient had an episode of unconsciousness, followed by inability to use the left leg.

Examination.—There were hyperactive reflexes, loss of abdominal reflexes, a bilateral Babinski sign and a questionable Chaddock sign on the right side.

Course.—On Oct. 1, 1937 examination showed left-sided hyperreflexia, absence of the Babinski sign, positive Mendel-Bechterew and Rossolimo signs on the left and weakness of the left upper and lower extremities. The duration of motor symptoms was five years.

Autopsy.—A small area of softening in the right cerebellar hemisphere involved the lobulus ansiformis crus II. There was a slight area of softening in the right paracentral lobule.

Microscopic Diagnosis.—The diagnosis was embolism of the paracentral branch of the right middle cerebral artery and branches of the posterior inferior cerebellar artery.

Examination of Pyramids.—There was no observable loss of axons in the pyramidal tract.

CASE 3.—A man aged 60 was admitted Feb. 24, 1939 and died Jan. 12, 1940.

History.—The patient had noted weakness of the left arm and leg for the past six months.

Examination.—At the time of admittance examination revealed essentially no motor deficit.

Course.—On Nov. 1, 1939, the patient was suddenly unable to talk; the right corner of his mouth drooped, and he was unable to move his right arm and leg. The weakness of the right upper extremity was of flaccid type. Ankle clonus was elicited on the right side. Abdominal reflexes were absent on the right. The Oppenheim sign was present on the right side but no other pathologic plantar responses were elicited. There was weakness of the right side of the face of central type. The aphasia improved somewhat.

The duration of symptoms was seven months.

Autopsy.—An area of softening was found in the posterior part of the third frontal convolution, at the base of the premotor, motor and parietal convolutions and possibly in part of the superior temporal convolution on the left side. Microscopic examination verified the gross observation and, in addition, showed that the island of Reil, the external capsule, the putamen and part of the internal capsule on the same side were also involved. The gray and the white matter were equally affected. The microscopic diagnosis was thrombosis of the left middle cerebral artery and branches of the left posterior cerebral artery, as well as generalized cerebral arteriosclerosis.

Examination of the Pyramids.—Silver-stained sections revealed no observable fiber loss.

CASE 4.—A woman aged 53 was admitted on June 4, 1940 and died November 12.

History.—Four weeks before admission the patient awoke in the morning and found her right arm and leg were weak.

Examination.—There were slight flaccid paresis of the right extremities, defective plantar responses bilaterally and absence of abdominal reflexes.

Course.—The duration of motor symptoms was seven months.

Autopsy.—There was a small area of softening in the region of the pulvinar of the thalamus on the left side. Microscopically, some of the fibers between the pulvinar and the medial lemniscus were completely destroyed. Fibers emerging from the dentate nucleus showed fragmentation, swelling and disintegration of myelin.

The microscopic diagnosis was thrombosis of a branch of the left posterior cerebral artery and emboli to branches of the superior cerebellar artery.

Examination of the Pyramids.—There was no evidence of a degenerative process in the axis-cylinders.

CASE 5.—A man aged 64 was admitted on June 20, 1936 and died on April 6, 1941.

History.—A staggering gait developed in March 1936, three months before the patient's admission. Shortly afterward the patient noted that the left upper and lower extremities were weak and that the mouth was drawn to the right. He was hospitalized for six weeks, during which time there was some increase in power on the left side. After his discharge his left extremities became weaker.

Examination.—Examination revealed left hemiparesis, impairment of skilled movements in the left hand, deep hyperreflexia on the left side; absence of the abdominal reflexes; Babinski, Chaddock, Oppenheim and Rossolimo signs on the left; a questionable Babinski sign on the right; slight paresis of the muscles of the jaw on the left side; paresis of the left lower part of the face; paresis of the left half of the palate, and deviation of the tongue to the left on protrusion.

Course.—On April 5, 1941, one day before his death, it was noted that the hemiplegia was marked on the left side.

The duration of motor symptoms was five years.

Autopsy.—A massive hemorrhage was present in the right cerebral hemisphere, involving essentially the white matter along the island of Reil and destroying practically all of it, the external capsule, the claustrum, the putamen, part of the internal capsule and part of the thalamic nuclei. There were hemorrhages in the tegmentum, extending from the aqueduct to the fourth ventricle, which was filled with hemorrhagic material.

Microscopic Diagnosis.—The diagnosis was hemorrhage or rupture of the right middle cerebral artery and branches of the basilar arteries; thrombosis of the left posterior inferior cerebellar artery; subarachnoid and intraventricular hemorrhages, and generalized cerebral arteriosclerosis.

Examination of the Pyramid.—There was no evidence of degeneration in the axons of the pyramidal tract.

CASE 6.—A man aged 59 was admitted June 26, 1936 and died June 29.

History.—The chief complaint of the patient was staggering gait. On Jan. 2, 1936, more than six months prior to admission, the patient experienced loss of consciousness and paralysis of the right side of the tongue. He was unable to stand for several days. On January 24 he was able to walk, with a staggering gait. On June 26, there was a repetition of the stroke and he was admitted to the hospital in a critical condition.

The duration of symptoms was seven months.

Autopsy.—A spherical cystic lesion, 8 mm. in diameter, occurred at the junction of the anterior and the posterior arm of the left internal capsule and extended into the lateral nucleus of the thalamus. A second, oval, cyst, 8 by 3 by 4 mm., was located in the centrum ovale of the right frontal lobe, just lateral to the corpus callosum. A third cyst, smaller than the second, was found just beneath the tip of the frontal horn of the left ventricle. All these cysts appeared not to be of recent origin.

Examination of the Pyramids.—No loss of axons in the pyramidal tract was observed.

CASE 7.—A man aged 47 was admitted with the chief complaint of right-sided hemiparesis on July 30, 1937 and died August 23.

History.—In May 1936, fourteen months prior to admission, the patient was found unconscious, with complete paralysis and inability to speak. Three weeks later speech and motor power began to return.

Examination.—There was clubbing of the fingers. The right arm was adducted, whereas the gait was normal. Associated movements of the right arm were almost absent. The right arm was atonic and flaccid. Speech was halting and thick. The abdominal reflexes were absent on the right side. No other abnormality of the reflexes was noted.

The duration of symptoms was fourteen months.

Autopsy.—Encephalomalacia involved the precentral, the postcentral and the posterior end of the superior frontal gyrus on the left side. Microscopic examination showed complete disappearance of the ganglion cells. There were no changes of note in the pons or the medulla. The probable diagnosis was embolus of the middle cerebral artery. The Betz cells may have been preserved.

Examination of the Pyramids.—No loss of axons was noted.

CASE 8.—A woman aged 51 was admitted Sept. 3, 1937, with staggering gait. She died October 8.

History.—In September 1936 there were noted wabbling gait and weakness of both lower extremities, with increased fatigability. By December 1936 she could walk only with support and since then had fallen a number of times when trying to walk.

Examination.—The patient was able to walk only with support, and then on a wide base and with marked unsteadiness. There was slight clumsiness of both hands, the left being more affected than the right. A Babinski sign was elicited on the right.

Course.—A suboccipital craniotomy was performed on Oct. 4, 1937.

The duration of symptoms was one year.

Autopsy.—The only observations of note were hemorrhage and vacuolation in the reticular formation of the midbrain and the pons.

Examination of Pyramids.—No loss of axons was noted.

CASE 9.—A man aged 59 was admitted Dec. 20, 1938 and died Jan. 3, 1939.

History.—The patient had had a stroke involving the right side one year before admittance to the hospital. Strength had gradually but never completely returned.

Examination.—There were paresis of the right side of the face and partial paralysis of the left side of the face of central type. The patient could move his left arm only slightly and could not grip with the left hand. He moved the right arm fairly well but with definite weakness. There was weak motion in both legs, the left being affected more than the right. Muscular tone was increased bilaterally. The tendon reflexes were increased. The abdominal reflexes were absent on the left. The cremasteric reflexes were absent. All pathologic toe signs were present bilaterally.

Course.—A second stroke occurred the night before death.

The duration of motor symptoms was one year.

Autopsy.—There was an old area of softening in the left inferior frontal gyrus. A similar area of old softening, corresponding to that described on the surface, involved the right precentral gyrus and the adjacent inferior frontal gyrus. A third area of old encephalomalacia, measuring approximately 1 by 0.25 cm. in cross section and 1.5 cm. anteroposteriorly, was present in the posterior extremity of the left putamen. It was cystic and light brown. There were no changes of note in the midbrain, pons or medulla.

Examination of the Pyramids.—There was no evidence of degeneration of axons in the pyramidal tract.

CASE 10.—A woman aged 53 was admitted July 17, 1939.

History.—Weakness of the left side of the body followed an operation for hysterectomy four months prior to her admission. Shortly after the operation left hemiplegia developed; this condition steadily improved.

Examination.—There were almost complete paralysis of the left arm and paresis of the left leg. No changes were noted in the deep reflexes, and the Babinski sign was not elicited.

Course.—During the patient's stay in the hospital, the left hemiplegia gradually disappeared. She died Sept. 14, 1939, about two months after admittance.

The duration of symptoms was six months.

Autopsy.—The white matter of the right cerebral hemisphere contained a few small zones of cystic malacia, and in these areas there was partial destruction of neural and glial elements.

Examination of the Pyramids.—There was no evidence of loss of axons in the pyramidal tract.

CASE 11.—A woman aged 52 was admitted with left-sided weakness on Sept. 25, 1941 and died October 15.

History.—In the fall of 1940 there developed weakness of the left lower limb and awkwardness of the left hand, which persisted and grew progressively worse.

Examination.—The gait was unsteady, and the patient was unable to walk on the heels or the toes. There was slight weakness of the left upper limb. Ankle clonus and a Babinski sign were elicited on the left. The deep reflexes were overactive bilaterally, and the abdominal reflexes were reduced bilaterally.

Course.—On Oct. 9, 1941, the patient was unable to walk, and the left hemiplegia became more pronounced.

The duration of symptoms was about one year.

Autopsy.—A macerated area occupied the right superior parietal lobule, the dorsal extremity of the transverse occipital gyrus and the cuneus. Hemorrhage into this area was observed. There was a herniation of the gyrus cingulus. The cerebral peduncles were displaced slightly toward the left. No changes of note were observed in the nuclei or the tracts of the medulla or pons. The cerebellar tonsils were herniated through the foramen magnum.

Examination of the Pyramids.—No degeneration of axons was noted.

COMMENT

If destruction of pyramidal tract fibers is the predominant cause of hemiparesis or hemiplegia, then I believe that it requires little or no loss of fibers of this tract to produce this symptom complex. This conclusion is based on the results of study of the pyramidal tract fibers in the pyramids in about 260 cases of paralysis caused by cerebral tumors and cerebrovascular injuries. Complete destruction of the pyramidal tract fibers in such cases is the exception rather than the rule. There are relatively many more cases in which there is no evidence of destruction. In the present series of 106 cases of vascular lesions, complete destruction occurred in 7, partial and variable loss of fibers in 36 and no microscopic evidence of a degenerative process in the pyramids in the remaining 63 cases.

There is abundant evidence in the literature that the pyramidal tract is one of the most delicate and susceptible tracts in the central nervous system. This viewpoint was originally expressed by the Netherland school of neurologists, and it has been correlated with the late phylogenetic and ontogenetic development of the bundle. From the evidence at hand, it would appear that the pyramidal tract fibers are difficult to destroy completely. If this is true, this tract should be a durable group of fibers. This does not mean that its physiology may not be interfered with when no destruction is discernible. Inhibition of nerve conduction may possibly be a factor in causing neural dysfunction.

An important question in neuropathology would seem to be the length of time it requires for disappearance of pyramidal tract fibers in man after maximum injury of their cells of origin or of their nerve fibers. Different pathologic processes might affect nerve fibers differently,

one pathologic entity destroying rapidly and another more slowly. Thrombosis, embolism and hemorrhages in themselves might not act in the same way in this respect. I have a case, recorded as one of complete left hemiplegia, in which the pyramidal tract is shown to have been completely destroyed five weeks after the onset of symptoms. In this laboratory, my colleagues and I have obtained rather complete degeneration of pyramidal fibers in the pyramids in the monkey in nineteen days and in the cat in six days after large scale removal of the cortex. Again, experimental cortical ablation may be an entirely different process than that which occurs in cases of cerebral tumor or vascular disease. I wish to be cautious and conservative in analyzing the pathologic data for man.

It is difficult to say what the exact role of the pyramidal tract is in total hemiplegia or complete paralysis. In many cases of cerebral tumors and cerebrovascular disease with chronic motor deficit in the striated muscles there is no overt evidence of destruction of the pyramidal tract. Cases of repeated strokes which produce transient hemiplegias likewise may fall into this category. Whether the neurons have not been involved in the pathologic process, whether they have survived the direct effects of the lesion or whether temporary or relatively lasting inhibition of neural activity over the pyramidal bundle may be factors, I am unable to say.

It is realized that there may be certain limitations involved in the material used in the investigation. Many observers participated in working out the histories, in giving the neurologic examinations and in analyzing the pathologic

data. It may be that in most instances their attention was not focused directly on the pyramidal tract. In the absence of any investigations limited directly to the problem, it is believed that the over-all observations may be suggestive that massive or all-inclusive neuronal destruction of the pyramidal tract is not the main pathologic factor in the majority of cases of paralysis. It is hoped that further investigations in suitable neurologic centers may be carried out in this field, special attention being paid to the extent and nature of the lesion in the region of the known elements of the pyramidal system.

SUMMARY AND CONCLUSIONS

Hemiparesis or hemiplegia, caused by chronic vascular lesions, can occur with little or no destruction of the fibers of the pyramidal tract.

In a series of 106 persons who died of cerebrovascular disease, 7 showed complete destruction of the axons within the pyramid, 36 exhibited varying amounts of degeneration and 63 gave no overt evidence of a degenerative process.

Patients having transient hemiplegias during life due to vascular insults may exhibit no loss of fibers of the pyramidal tract post mortem. This may explain, in part, the restitution of function in these patients.

In general, cerebrovascular lesions produce more destruction of axons of the pyramidal tract than do cerebral tumors.

In contrast to the prevailing opinion, the neurons of the pyramidal tract appear to be durable and difficult to destroy completely.

Medical College of the State of South Carolina 16.

BILATERAL INTRACRANIAL SECTION OF THE GLOSSOPHARYNGEAL NERVE

REPORT OF A CASE

HENRY WYCIS, M.D.

PHILADELPHIA

Unilateral intracranial division of the glossopharyngeal nerve is indicated in cases of glossopharyngeal tic, hypersensitive carotid sinus syndrome and malignant growths of the nasopharynx.

A case of glossopharyngeal pain was first recorded by Weisenburg,¹ in 1910. Autopsy in this case disclosed a tumor of the posterior fossa involving primarily the ninth cranial nerve. In 1920 Sicard and Robineau² recorded 3 cases of true glossopharyngeal neuralgia. They asserted that the pain was due to involvement of the ninth and tenth cranial nerves and the superior cervical sympathetic ganglion. In 1921 Harris³ introduced the term glossopharyngeal neuralgia and described 2 cases. A great deal of confusion arose at this time as to whether the glossopharyngeal nerve was motor or sensory or both. Vernet⁴ taught that the glossopharyngeal nerve was largely motor in function and that sensation to the pharynx and soft palate was supplied by the vagus nerve. Dandy,⁵ in 1927, showed that by intracranial division of the ninth cranial nerve glossopharyngeal pain could be relieved. He attempted to demonstrate that the glossopharyngeal nerve was entirely sensory and that it supplied the nasopharynx, the posterior pharyngeal wall to the epiglottis, the tonsil, the soft palate and the posterior third of the tongue. The salivary glands receive a parasympathetic

motor outflow, and it was shown by Reichert and Poth⁶ that after section of the glossopharyngeal nerve temporary suppression of salivation resulted. Because of Vernet's teaching, Sicard and Robineau,² Doyle⁷ and Adson⁸ sectioned the ninth and tenth cranial nerves and sympathetic nerves. It remained for Dandy⁵ to outline the rational treatment for glossopharyngeal tic, although Adson had planned such a procedure three years earlier. Since the introduction of Dandy's operation, numerous neurosurgeons have adopted the procedure for relief of glossopharyngeal tic. The trigger zone in cases of this disorder lies in the tonsillar area, although in occasional cases a second trigger point may be found in the external auditory canal. In such instances it is apparently necessary to section not only the glossopharyngeal nerve but the superior rootlets of the vagus nerve. Such cases have been reported by McKenzie and Keith⁹ and by Spurling and Grantham.¹⁰

Since the pioneer work by Weiss and Baker¹¹ in 1933 on the hypersensitive carotid sinus syndrome, several reports¹² have appeared in the

From Temple University Hospital and Medical School.

1. Weisenburg, T. H.: Cerebello-Pontile Tumor Diagnosed for Six Years as Tic Douloureux: The Symptoms of Irritation of the Ninth and Twelfth Cranial Nerves, *J. A. M. A.* **54**:1600-1604 (May 14) 1910.

2. Sicard, R., and Robineau: I. Algie vélo-pharyngée essentielle: Traitement chirurgical, *Rev. neurol.* **37**:256-257, 1920.

3. Harris, W.: Persistent Pain in Lesions of the Peripheral and Central Nervous System, *Brit. M. J.* **2**:896-900, 1921.

4. Vernet, M.: Syndrome du trou déchire postérieur (Paralysie des nerfs glossopharyngeal, pneumogastrique, spinal), *Rev. neurol.* **34**:117, 1918.

5. Dandy, W. E.: Glossopharyngeal Neuralgia (Tic Douloureux): Its Diagnosis and Treatment, *Arch. Surg.* **15**:198-214 (Aug.) 1927.

6. Reichert, F. L., and Poth, E. J.: Pathways for the Secretory Fibers of the Salivary Glands in Man, *Proc. Soc. Exper. Biol. & Med.* **30**:973-977, 1933.

7. Doyle, J. B.: A Study of Four Cases of Glossopharyngeal Neuralgia, *Arch. Neurol. & Psychiat.* **9**:34-46 (Jan.) 1923.

8. Adson, A. W.: The Surgical Treatment of Glosso-Pharyngeal Neuralgia, *Arch. Neurol. & Psychiat.* **12**:487-506 (Nov.) 1924.

9. McKenzie, K. G., and Keith, W. S.: Report read before the Harvey Cushing Society, 1938.

10. Spurling, R. G., and Grantham, E. G.: Glossopharyngeal Neuralgia, *South. M. J.* **35**:509-513, 1942.

11. Weiss, S., and Baker, J. P.: The Carotid Sinus Reflex in Health and Disease: Its Role in Causation of Fainting and Convulsions, *Medicine* **12**:297-354, 1933.

12. (a) Bucy, P. C.: Carotid Sinus Nerve in Man, *Arch. Int. Med.* **58**:418-432 (Sept.) 1936. (b) Craig, W. M., and Smith, H. L.: The Surgical Treatment of Hypersensitive Carotid Sinus Reflexes: Thirteen Cases, *Yale J. Biol. & Med.* **11**:415-422, 1939. (c) Herbert, C.; Zahn, D.; Ryan, J., and Echlin, F.: Treatment of Carotid Sinus Sensitivity by Intracranial

(Footnote continued on next page)

literature dealing with surgical therapy of this entity. Weiss, Capps, Ferris and Munro¹³ denervated the carotid sinus in 10 patients. They demonstrated a temporary, but distinct, increase in heart rate and blood pressure in their patients following this procedure. They had no opportunity to observe the effect of bilateral denervation on the level of the blood pressure. Unilateral intracranial section of the glossopharyngeal nerve for relief of the symptoms due to a hypersensitive carotid sinus has been reported on by Herbert, Zahn, Ryan and Echlin^{12c} and by Ray and Stewart.^{12d} The first group of workers stated the belief that intracranial section of the glossopharyngeal nerve completely denervated the carotid sinus, while Ray and Stewart showed conclusively that even after intracranial section of the ninth nerve procainization of the carotid sinus still caused a rise in blood pressure (2 cases). Of the 4 cases reported by Ray and Stewart, a temporary rise in blood pressure occurred in 3, while no significant changes appeared in the fourth case.

Section of the glossopharyngeal nerve for the relief of pain in the throat due to a malignant growth was first suggested and carried out by Fay.¹⁴ This was in 1926, and use of the method for this purpose preceded Dandy's operation for glossopharyngeal tic. The procedure of intracranial section of the fifth and ninth cranial nerves and posterior cervical rhizotomy offers relief of pain in cases of malignant growths of the nasopharynx.

After the original investigation of Ludwig and Jarisch¹⁵ on the depressor nerve and of Hering¹⁶ on the carotid sinus, Koch and Mies¹⁷

were able to demonstrate hypertension in experimental animals following bilateral section of the carotid sinus and the aortic depressor nerves (moderator nerves). The release of the cardiac and vasomotor centers from the influence of the moderator nerves permits these centers to exert a greater degree of cardiac acceleration and vasoconstriction. Not only had Heymans¹⁸ confirmed this work, but he was able to produce and maintain arterial hypertension of 250 to 300 mm. of mercury for periods of nine to twenty-six months by section of the moderator nerves in dogs. Nowak and Walker¹⁹ have reported an elevation of arterial blood pressure in dogs for as long as three years. The degree and duration of the hypertension depend, apparently, on the extensiveness of the operative procedure. Green, DeGroat and McDonald,²⁰ using a similar operative technic, were unable to duplicate Heymans' results in rabbits and dogs. Heymans stated that the failure to produce permanent hypertension in all dogs was due to the presence of accessory fibers in the cardio-aortic nerves and to the presence of moderator, depressor influence in the pulmonary and intestinal pressor nerves. Complete removal of the paravertebral ganglionic chain can prevent or abolish this type of experimental hypertension (Heymans^{18b}). It is of interest to note that the blood of these hypertensive dogs has a higher degree of vasopressor activity than has that of normal controls (Heymans and Bouckaert²¹).

In man, Bucy^{12a} was the first person to demonstrate hypertension by intracranial division of the glossopharyngeal nerve. Ask-Upmark,²² a year earlier, had demonstrated a sharp and immediate rise in blood pressure following denervation of the carotid sinus. However, he had failed to make any prolonged observations in his

Section of the Glossopharyngeal Nerve, Tr. Am. Neurol. A. **68**:29-31, 1942. (d) Ray, B. S., and Stewart, H. J.: Observations and Surgical Aspects of the Carotid Sinus Reflex in Man, Surgery **11**:915-938, 1942.

13. Weiss, S.; Capps, R. B.; Ferris, E. B., Jr., and Munro, D.: Syncope and Convulsions Due to Hyperactive Carotid Sinus Reflex: Diagnosis and Treatment, Arch. Int. Med. **58**: 407-417 (Sept.) 1936.

14. Fay, T.: Intracranial Division of Glossopharyngeal Nerve Combined with Cervical Rhizotomy for Pain in Inoperable Carcinoma of the Throat, Ann. Surg. **84**:456-459, 1926.

15. Ludwig, W., and Jarisch, A.: Ueber die Wirkung des N. depressor mit besonderer Berücksichtigung der Beteiligung des Herzens, Arch. f. exper. Path. u. Pharmacol. **114**:240-251, 1926.

16. Hering, H. E.: Die Karotissinusreflexe auf Herz und Gefässe vom normal-physiologischen, pathologisch-physiologischen und klinischen Standpunkt. Gleichzeitig über die Bedeutung der Blutdruckzügler für den normalen und abnormen Kreislauf, Dresden, Theodor Steinkopff, 1927.

17. Koch, E., and Mies, H.: Chronischer arterieller Hochdruck durch experimentelle Dauerausschaltung der Blutdruckzügler, Krankheitsforschung **7**:241-256, 1929.

18. (a) Heymans, C.: Les fonctions réflexogènes de l'aorte et du sinus carotidien, Compt. rend. Soc. de biol. **107**:1293-1330, 1931; (b) Some Aspects of Blood Pressure Regulation and Experimental Arterial Hypertension, Surgery **4**:487-501, 1938.

19. Nowak, S. J. G., and Walker, I. J.: Experimental Studies Concerning Nature of Hypertension: Their Bearing on Surgical Treatment, New England J. Med. **220**:269-274, 1939.

20. Green, M. F.; DeGroat, A. F., and McDonald, C. H.: Observations on Denervation of the Carotid Sinuses and Section of the Depressor Nerves as a Method of Producing Arterial Hypertension, Am. J. Physiol. **110**:513-520, 1935.

21. Heymans, C., and Bouckaert, J. J.: Observations chez le chien en hypertension artérielle chronique et expérimentale, Compt. rend. Soc. de biol. **106**:471-473, 1931.

22. Ask-Upmark, E.: The Carotid Sinus and the Cerebral Circulation: Anatomical, Experimental, and Clinical Investigation, Including Some Observations on the Rete Mirabile Caroticum, Acta psychiat. et neurol., 1935, supp. 6, pp. 1-374.

cases. In 4 of the 5 cases reported by Bucy, a rise in blood pressure persisted for six to fourteen days. Ray and Stewart^{12d} likewise observed a temporary rise in blood pressure in 4 cases after unilateral intracranial division of the glossopharyngeal nerve.

Bilateral denervation of the carotid sinus in man has been reported in the European literature by Lauwers,²³ Danielopolu²⁴ and Leriche, Fontaine and Froehlich.²⁵ These investigators reported no serious after-effects or any significant permanent changes in blood pressure. In this country the late effects of bilateral denervation of the carotid sinus in man, particularly the vascular reflexes, were studied in 2 cases by Capps and de Takáts.²⁶ They found that bilateral denervation of the carotid sinus in man failed to produce a permanent elevation of blood pressure and could result in postural hypotension, as shown in their 2 cases. The postural hypotension was explained as being due to a relatively lower sensitivity of the aortic depressor mechanism than that of the carotid sinus.

The literature reveals no case of bilateral intracranial division of the glossopharyngeal nerve in man. The present case is therefore reported because of its significance in the study of the vascular reflexes and because of the value of the procedure in the relief of pain in the throat radiating to both ears due to a malignant growth in the nasopharyngeal region.

REPORT OF CASE

History.—Mr. J. T., aged 51, was admitted to the service of Dr. W. E. Chamberlain at Temple University Hospital on Jan. 12, 1945, with a diagnosis of squamous cell carcinoma of the epipharynx. Prior to admission he had had a course of roentgen irradiation to both sides of the neck and implantation of radium into the epipharyngeal area. His chief complaint was a deep-seated pain in the throat, which radiated to both ears, being more pronounced on the right side. He also had a pain which began over the left mastoid process and radiated upward above the ear. Since the roentgen therapy he had had bilateral pain in the neck, presumably due to irradiation neuritis. There was trismus of the jaws, so that it was difficult for him to take any but liquid nourishment. The general physical and neurologic examination otherwise showed nothing significant. Pressure on the carotid sinus on either side failed to produce any appreciable slowing of the

heart. The electrocardiogram was normal. In view of the bilateral cervical pain and the excruciating bilateral pain in the throat, it was decided to do a posterior cervical rhizotomy and bilateral intracranial section of the glossopharyngeal nerve. The patient was, accordingly, transferred to the neurosurgical service for operation.

Operation (Jan. 19, 1945).—High cervical laminectomy, with removal of the rim of the foramen magnum, was performed, using local anesthesia.

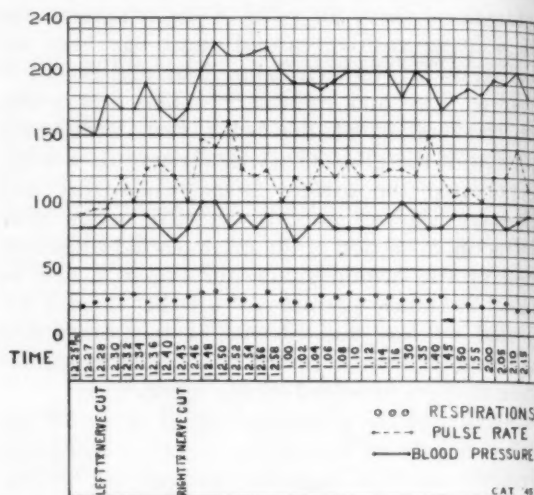


Fig. 1.—Observations on the pulse, respiration and blood pressure recorded by the anesthetist during operation. Note the immediate responses on section of each glossopharyngeal nerve.

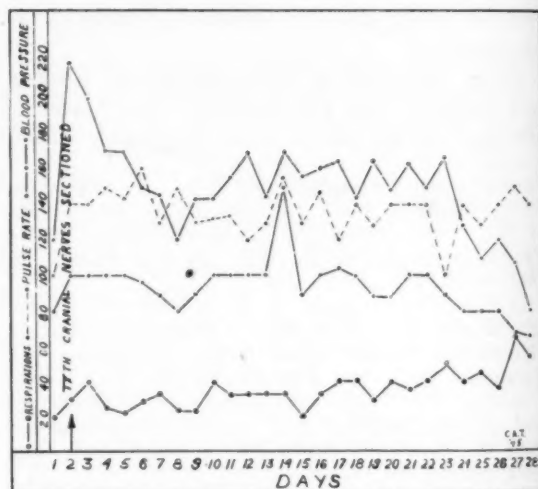


Fig. 2.—Observations on the pulse, respiration and blood pressure of the patient for a period of four weeks following operation. Note the persistent elevation of blood pressure except for five days prior to his death.

23. Lauwers, E. E.: L'extirpation du corpuscule carotidien dans l'épilepsie, *J. de chir.* **37**:686-702, 1931.

24. Danielopolu, D.: Sur la pathogénie de l'épilepsie et sur son traitement chirurgical, *Presse méd.* **41**:170-174, 1933.

25. Leriche, R.; Fontaine, R., and Froehlich, F.: L'énervation sinu-carotidienne, *Presse méd.* **43**:1217-1220, 1935.

26. Capps, R. B., and de Takáts, G.: The Late Effects of Bilateral Carotid Sinus Denervation in Man: A Report of Two Cases with Studies of the Vascular Reflexes, *J. Clin. Investigation* **17**:385-389, 1938.

The laminas of the first to the fourth cervical vertebrae inclusive were removed. The posterior margin of the foramen magnum was rongéured away. The posterior roots of the first to the fourth cervical nerves inclusive were clipped and divided. With some difficulty, the cerebellum was retracted, exposing the ninth, tenth and eleventh cranial nerves on the left

side. The preoperative blood pressure was 122 mm. of mercury systolic and 80 mm. diastolic. The pulse rate was 110 and the respiratory rate 20, per minute. Just prior to section of the left ninth nerve the record was as follows: pulse rate, 80 per minute; respiratory rate, 20 per minute, and blood pressure, 150 mm. systolic and 80 mm. diastolic. Immediately on section of the left ninth nerve, the pulse rate rose to 90 and the respiratory rate to 26, per minute; the blood pressure rose suddenly to 180 mm. systolic and 90 mm. diastolic (fig. 1). During the next fifteen minutes the blood pressure oscillated from 160 systolic and 70 diastolic to 190 systolic and 90 diastolic. At the end of fifteen minutes the right ninth nerve was cut. The response was immediate and dramatic. The pulse rate rose to 144 and the respiratory rate to 30, per minute. The blood pressure rose to 220 systolic and 100 diastolic (fig. 1). During the remainder of the operation the pulse rate varied from 100 to 160 per minute. The respiratory rate varied from 20 to 30 per minute. The blood pressure continued to be high and ranged from

branes. There was sensory loss to all modalities over an area corresponding to the distribution of the upper four cervical dermatomes. The patient was completely free of all pain. Unfortunately, bronchopneumonia and aspiration atelectasis developed. Bronchoscopic aspirations had to be done on several occasions. Dr. Charles Norris, who did the aspirations, noted free movement of both vocal cords. The sloughing mass in the epipharynx continued to feed the lungs below, and the patient finally died of suppurative pneumonitis, one month after operation.

Autopsy (February 15).—The brain was removed without disturbing the brain stem. The brain stem was carefully retracted, exposing the operative sites, where the ninth nerves had been cut (fig. 3). A small neoplasm, about the size of a cherry, was found projecting into the tip of the petrous portion of the right temporal bone. The surrounding area was a great mass of slough, which was due to irradiation necrosis. The lungs showed suppurative pneumonitis. The kidneys revealed cloudy swelling but no significant hypertensive changes.



Fig. 3.—Autopsy specimen, showing the position of the sectioned glossopharyngeal nerve on the right and left sides. The arrows point to the divided nerve ends.

190 systolic and 90 diastolic to 220 systolic and 100 diastolic (fig. 1).

For two hours after the operation the blood pressure remained between 170 systolic and 98 diastolic and 198 systolic and 100 diastolic and then fell to 160 systolic and 40 diastolic. During the next three days the blood pressure varied from 140 systolic and 80 diastolic to 168 systolic and 105 diastolic. The pulse ranged from 130 to 160 beats per minute and the respiratory rate from 20 to 36 per minute (fig. 2). The hypertension continued for four weeks, and the blood pressure did not reach preoperative levels until five days prior to the patient's death, when he showed signs of failing circulation (fig. 2).

Immediately after operation there was no dysphagia, and the patient could swallow liquids without choking. It was difficult to open his jaws because of the trismus, but it was noted that the gag reflex was absent bilaterally and that there was loss of sensation to pin prick and deep pressure over the posterior pharyngeal wall. The patient had definite sensation to pain in both auditory canals and over both tympanic mem-

COMMENT

A case is presented for the first time in which both ninth nerves were sectioned intracranially. The response of the blood pressure was immediate and dramatic and persisted until the patient's death, four weeks later. Pain in the throat with radiation to both ears is extremely distressing and cannot be relieved by unilateral section of the ninth nerve. The patient in this case was completely relieved of pain after bilateral section of this nerve. Bilateral section of the ninth nerve leaves the patient with an anesthetic pharynx and absence of the gag reflex. This condition should be compatible with life, provided the patient does not have a sloughing epipharyngeal mass which feeds the trachea below.

Temple University Hospital.

MULTIPLE SCLEROSIS WITH LATE ONSET OF SYMPTOMS

ARNOLD P. FRIEDMAN, M.D.

AND

CHARLES DAVISON, M.D.

NEW YORK

The onset of symptoms in multiple sclerosis usually occurs between the second and the fourth decade of life. Its diagnosis, with few exceptions, is rarely entertained when signs of involvement of the central nervous system make their appearance in the fifth or the sixth decade of life. Wilson,¹ in a series of 1,107 cases of multiple sclerosis, found onset of symptoms after the age of 40 in 186, or 17 per cent, while von Hoesslin² found onset after the age of 50 in only 4 per cent. In many of the aforementioned cases the diagnosis was not verified by autopsy. Isolated examples of a very late onset with autopsy include Nielsen's³ case, in which illness began in the late sixties, and Taga's⁴ cases, in which the disease began after the age of 60.

In a series of 310 patients with multiple sclerosis who had been admitted to the Montefiore Hospital since 1922, the onset of symptoms after the age of 40 occurred in 41, or 13 per cent. Of the 42 patients on whom autopsy was performed, 9 (21 per cent) had the onset of symptoms after the age of 40. Because of the late onset, the diagnosis of multiple sclerosis was made before death for only 2 of the 9 patients. The case histories of these 9 patients have been studied in order to determine whether the symptoms and clinical course of the patients with a late onset of symptoms differs from that of patients with an onset early in life. The results are presented in the hope that they will be of value in establishing the diagnosis in other patients with late onset of symptoms.

From the Division of Neuropsychiatry, Montefiore Hospital, and the Department of Neurology, Columbia University College of Physicians and Surgeons.

1. Wilson, S. A. K.: *Neurology*, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940.

2. von Hoesslin, R.: *Ueber multiple Sklerose: Exogene Aetiologie, Pathogenese und Verlauf*, Munich, J. F. Lehmann, 1934.

3. Nielsen, J. M.: *A Textbook of Clinical Neurology*, New York, Paul B. Hoeber, Inc., 1940.

4. Taga, K.: *Zur Kenntnis der senilen multiplen Sklerose*, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **31**: 163, 1929.

REPORT OF CASES

CASE 1.—Onset of symptoms referable to the brain stem and spinal cord at age of 53. Diagnosis of cervical neoplasm. Death following laminectomy two months after onset of symptoms.

History.—R. M., a woman aged 53, was admitted to the Montefiore Hospital on June 8, 1937, with a history of numbness and weakness of the right upper extremity for two months. Soon after the onset of this symptom there appeared pain over the left side of the face, frontal headache and disturbance of vision in the left eye. A diagnosis of paranasal infection was made, and the symptoms disappeared after therapy. Weakness of both lower extremities and numbness of the left hand appeared. Her past illnesses included meningitis, in 1918, with residual deafness in the right ear, and arthritis of the lumbosacral region.

Examination.—The optic disks were normal. There were a Horner syndrome on the right, paralysis of the right upper and lower extremities and paresis of the left extremities. All deep reflexes were hypoactive and equal in the upper extremities. Ankle clonus and a Babinski reflex were elicited on the right side. The abdominal reflexes were absent. There was loss of pain and temperature sensation on the left side below the level of the third cervical dermatome.

Laboratory Data.—Examination of the blood and urine revealed nothing abnormal. The cerebrospinal fluid was under a pressure of 50 mm. of water. There was a prompt rise in pressure on jugular compression, but the fall in pressure was slow. These results were interpreted as indicating partial subarachnoid block. The fluid was clear and contained 7 lymphocytes per cubic millimeter and 66 mg. of protein per hundred cubic centimeters. A pronounced degree of spondylitis in the bodies of the cervical and thoracic vertebrae was shown roentgenographically.

Course.—On the basis of a presumptive diagnosis of tumor of the spinal cord, a laminectomy was performed under local anesthesia five days after the patient's admission. The cord was swollen, but no neoplasm was found. The postoperative course was stormy, and the patient died two days after operation.

Report of Autopsy.—A demyelinated plaque in the left occipital lobe destroyed part of the optic radiation and the white matter of the precuneus (fig. 1A). The myelin sheaths in this area showed all types of destruction. In the cresyl violet preparations the plaque was filled with numerous compound granular corpuscles, microglia cells and occasional gemastete glia cells. Perivascular collections of lymphocytes, plasma cells, endothelial cells and compound granular corpuscles were in abundance. Proliferation of the vessels was noted in places. The proliferated vessels showed thickening of all coats.

An occasional hyalinized vessel was also noted. In the Holzer preparations there was extensive gliosis in the area with loss in myelin. In the Bielschowsky preparation, the axis-cylinders showed slight destructive

The segments of the cervical portion of the cord were enlarged and contained a large demyelinated plaque, which destroyed the greater part of the cord (fig. 1 *B*). In one segment of the cervical region hardly any white

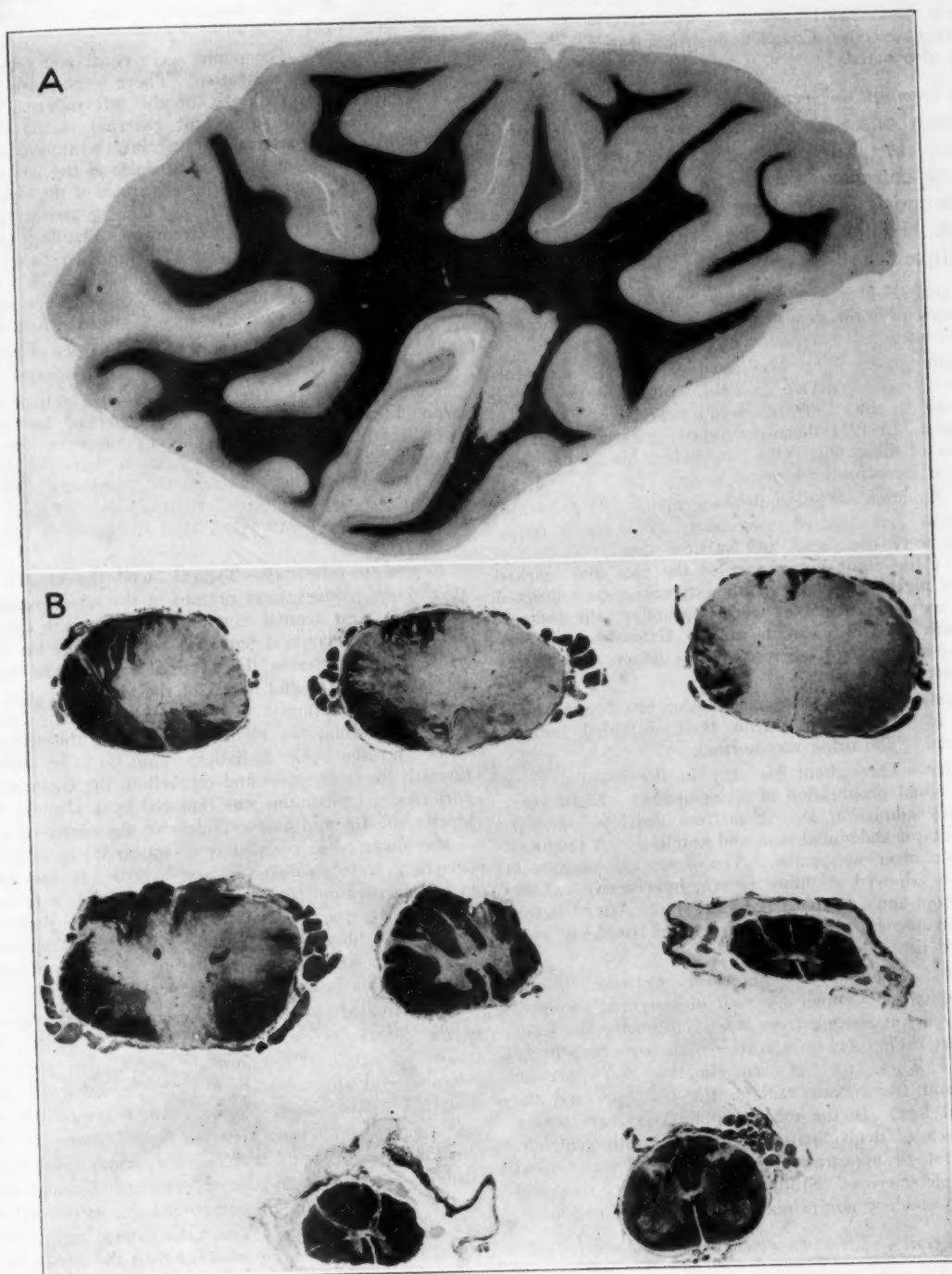


Fig. 1 (case 1).—Demyelinated area in the region of the optic radiation and white matter of the precuneus (*A*) and extensive plaque involving the cervical and upper thoracic regions (*B*). Notice that the middle lower thoracic and lumbar segments were spared. Myelin sheath stain.

changes, such as swelling, breaking down and a corkscrew appearance. Another plaque was found in the region of the cerebellar nuclei.

fibers were left. In the other sections some of the white fibers at the periphery of the cord were spared. There was no descending or ascending demyelination.

The microscopic picture was the same as that of the area in the occipital convolutions. In the Bielschowsky preparations, the axis-cylinders were fairly well preserved, but in places they were swollen and had a corkscrew appearance and bulbous processes. The ganglion cells were well preserved, but in some areas a few showed shrinkage and chromatolysis or appeared as shadow cells. Complete destruction of ganglion cells was also noted.

Comment.—Because of the patient's age, the sudden onset and rapid progression of symptoms, essentially limited to the cervical portion of the cord, and the partial subarachnoid block, a diagnosis of neoplasm of the spinal cord was made. Histologically the lesions were typical of multiple sclerosis.

CASE 2.—Onset of symptoms referable to the cerebellum and brain stem at age of 42. Progressive course, of fourteen years' duration.

History.—L. S., a man aged 47, entered the Montefiore Hospital on Oct. 25, 1914, with a history of bouts of dizziness since 1909, followed a year later by transient diplopia. In 1911 there developed staggering gait and tremor of the hands. One year before his admission he became incontinent of urine.

Examination.—The pupils were miotic and responded to light but reacted sluggishly in accommodation. There were horizontal and vertical nystagmus, weakness of the right lower part of the face and marked tremor of the head and of all extremities on volitional movement. The reflexes were hypoactive; the abdominal reflexes were absent, and a Babinski sign was elicited on the right. Sensation was intact. There was incontinence of urine.

Laboratory Data.—Studies of the blood and spinal fluid, including Wassermann tests, revealed nothing abnormal. The urine was normal.

Course.—Throughout his stay in the hospital there was gradual progression of all symptoms. Eight years after his admission gastric distress developed and he had bouts of abdominal pain and vomiting. A diagnosis of peptic ulcer was made. Neurologic examination at this time showed scanning speech, hyperactive reflexes throughout and a bilateral Babinski sign. After fourteen years in the hospital the patient died suddenly of a ruptured peptic ulcer.

Report of Autopsy.—There was extreme internal hydrocephalus. Numerous well demarcated demyelinated areas, measuring from a few millimeters to 1 cm. in diameter (fig. 2), were scattered through both hemispheres. These foci of demyelination were present throughout the corona radiata, the thalamus and the temporal lobe. In the medulla oblongata there was a large area of demyelination near the fourth ventricle. The histologic appearance of these plaques was typical of multiple sclerosis. Study of the spinal cord disclosed neither secondary nor primary foci of demyelination.

Comment.—This case offered no diagnostic difficulties, and multiple sclerosis was considered by all observers to be the most probable diagnosis.

CASE 3.—Onset of symptoms referable to the brain stem and spinal cord at age of 41. One remission of symptoms in an otherwise progressive course of twenty years' duration.

History.—F. F., a woman aged 58, was admitted to the Montefiore Hospital on July 19, 1923, with a history of diplopia and bouts of dizziness since 1906. There was a remission of symptoms for one year. In 1908 there developed weakness, followed by complete paralysis. In 1917 she began to have pains and weakness in the right upper extremity.

Examination.—The pupils were equal and reacted to light and in accommodation. There were ptosis of the right upper lid, paralysis of the left external rectus muscle, paresis of the right external rectus muscle, horizontal and vertical nystagmus, weakness of the lower right side of the face, atrophy of the left side of the tongue, dysarthria, flaccid paralysis of the right arm and leg, spastic paralysis of the left leg and atrophy of the muscles of both lower extremities. The deep reflexes were hypoactive and unequal. Abdominal reflexes were absent. A Babinski sign was present bilaterally. There was impairment of all modalities of sensation on the right side of the body. The mental status was normal.

Laboratory Data.—There was a faint trace of albumin in the urine. The cerebrospinal fluid was normal.

Course.—Shortly after admission the patient complained of difficulty in breathing and of hoarseness. This condition cleared up, but eight months later she experienced severe persistent pain on the right side of the jaw. Bronchopneumonia developed and she died thirty-nine months after entering the hospital, and approximately twenty years after the onset of the first symptom.

Report of Autopsy.—Typical, well demarcated demyelinated plaques were present in the white matter of the right first frontal convolution, the right centrum ovale, the insular and temporal convolutions, the right neostriatum bordering the external capsule, the fornix, the lateral and medial nuclei of the right thalamus, the gray and white matter of the postcentral convolutions, the right insula, the right hippocampus, the temporal lobes and the optic radiations (fig. 3). In sections through the brain stem and cerebellum the entire upper part of the tegmentum was replaced by a plaque. The myelin sheaths and axis-cylinders in the center of most of the plaques had completely disappeared; those at the periphery were swollen and fragmented. In the cresyl violet preparation the plaques were filled with rod-shaped microglia cells and astrocytes. At the periphery there were numerous gemistocyte glia cells. Occasional perivascular infiltrations, consisting of nuclei of compound granular corpuscles, were noted.

Demyelinated plaques were present in various regions of the spinal cord and involved the gray matter, the crossed and direct pyramidal tracts, the posterior columns and the ventral cerebellar, rubrospinal and spinothalamic pathways. Many of the nerve cells in the gray matter had been destroyed, and many of the remaining cells had undergone various pathologic changes, ranging from almost complete disappearance of the ganglion cells to neuronophagia, satellitosis or loss of Nissl substance. The anterolateral and anteromesial groups were more involved than the dorsolateral and dorsomesial groups.

Comment.—Although paralysis of ocular nerves and atrophy of the muscles of the tongue and the extremities are rare in cases of multiple sclerosis, the diagnosis of this disease was entertained by several of the examiners. One of us

Fig.
stain.

F
matt
stain



Fig. 2 (case 2).—Numerous demyelinated plaques scattered throughout the white matter. Myelin sheath stain.

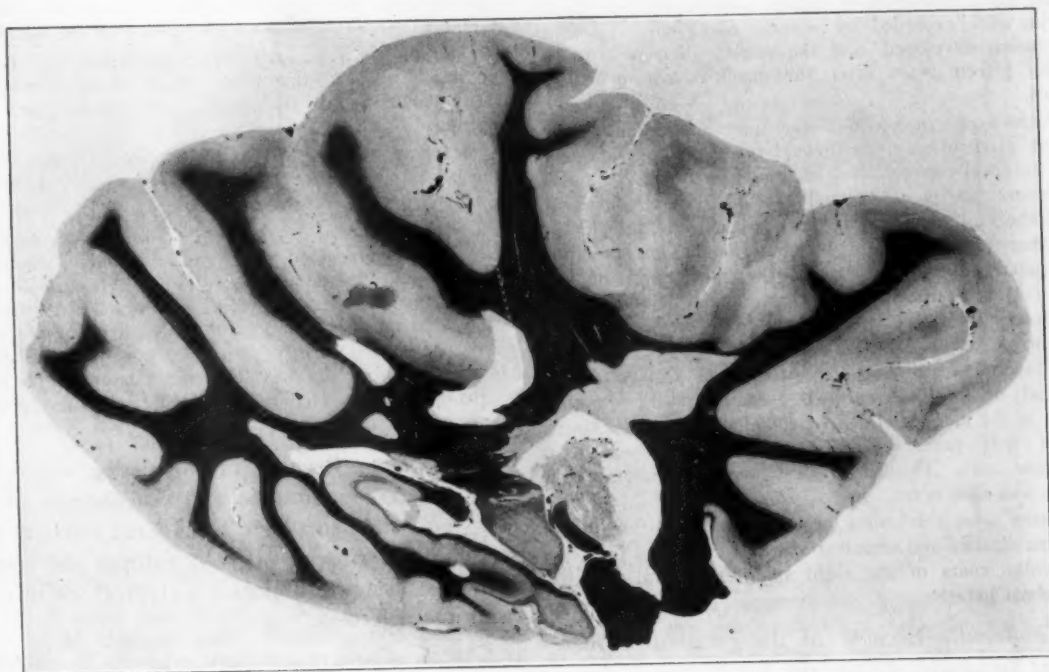


Fig. 3 (case 3).—Section through the temporal horn, showing demyelinated areas throughout the white matter, especially in the vicinity of the ventricle. Notice the small plaque in the hippocampus. Myelin sheath stain.

(Davison) and associates⁵ previously reported a series of cases of multiple sclerosis with changes in the anterior horn cell and atrophy of muscles.

CASE 4.—Onset at age of 43 with signs of involvement of the cerebellar and pyramidal tracts. Progressive course, with death after fifteen years.

History.—J. M., a man aged 54, a house painter, who was admitted to the Montefiore Hospital on July 5, 1935, had onset of periodic pain and cramps in his calves in 1923. About six months later he experienced weakness and unsteadiness of his legs, which progressed so that he was unable to walk without the use of a cane. In 1935 there appeared urgency in micturition, followed by weakness and unsteadiness of the upper extremities. About six months before his admission his handwriting became totally illegible.

Examination.—The pupils were irregular in outline but reacted well to light and in accommodation. There were horizontal nystagmus and hoarseness of the voice, and the gag reflex was absent. Muscular power was diminished in all extremities. The deep reflexes were active throughout. The abdominal reflexes were present, and there was a questionable Babinski sign on the right side. The gait had a wide base, and ataxia was present in all extremities but was more marked on the right side. The sensory examination was normal. There were evidences of intellectual deterioration.

Laboratory Data.—Studies of the blood and cerebrospinal fluid, including the Wassermann tests, gave normal results except for a protein content of the cerebrospinal fluid of 58 mg. per hundred cubic centimeters. The urine was normal.

Course.—The condition of the patient did not change greatly during his three year stay in the hospital, although dissociation of ocular movements and dysarthria were recorded by several observers. Coronary occlusion developed, and the patient died on July 17, 1938, fifteen years after the onset of the neurologic signs.

Report of Autopsy.—There were numerous discrete areas of demyelination throughout the white matter of the cerebral convolutions, in the right insula, the corpus callosum, the right internal capsule, the right pulvinar and the right substantia nigra, around the aqueduct of Sylvius (fig. 4 A and B), and in the left brachium conjunctivum, the left pyramid, the right dentate nucleus, the corpus restiforme, the right medial lemniscus and the cerebellum. In the spinal cord there was a plaque in the posterior columns. The microscopic changes of the myelin sheaths, axis cylinders and glia cells were typical of multiple sclerosis. Many of the ganglion cells in the plaques which extended into the gray matter were well preserved; some, however, appeared as shadow cells. Occasional destruction of the ganglion cells was also noted.

There were thickening of the intima, splitting of the lamina elastica and fenestration and thinning of the other muscular coats of the right middle cerebral and left vertebral arteries.

Comment.—Because of the pronounced cerebellar signs and dysarthria, the diagnosis during life was olivopontocerebellar atrophy. The signs

5. Davison, C.; Goodhart, S. P., and Lander, J.: Multiple Sclerosis and Amyotrophies, *Arch. Neurol. & Psychiat.* 31:270 (Feb.) 1934.

referable to the pyramidal tract were not considered to be significant by most of the examiners. Pathologically the lesions were typical of multiple sclerosis. Although there was evidence of arteriosclerosis in some of the cerebral vessels, there were no areas of softening. The atherosclerotic process occurred shortly before death.

CASE 5.—Onset of cerebral symptoms at age of 64. Death from uremia one year after onset of symptoms.

History.—S. P., a man aged 65, was admitted to the Montefiore Hospital on Dec. 22, 1932, with a history of frequent and painful urination since April 1931. A tentative diagnosis of nephrolithiasis was made. One year later he returned complaining of hematuria and pain in the perineum. A diagnosis of carcinoma of the bladder was made, and he received eight roentgen ray treatments. Personality changes and loss of memory had been noted for one year.

Examination.—The pupils reacted sluggishly to light and in accommodation. There were horizontal nystagmus, slight intention tremor bilaterally in the finger to nose test and hyperactive deep reflexes throughout. The patient's mood was labile and irritable. Speech was incoherent and irrelevant. He was poorly oriented, and memory for recent events was poor. Insight and judgment were defective. The blood pressure was 130 systolic and 70 diastolic. The prostate was enlarged and indurated.

Laboratory Data.—The urine was loaded with pus cells, and gave a 1 plus reaction for albumin. There was moderately severe hypochromic anemia. Roentgenograms of the pelvis and the spine revealed no evidence of metastasis. Wassermann reactions of the blood and the spinal fluid were negative. Examination of the cerebrospinal fluid revealed nothing remarkable. Cystoscopic examination showed a neoplasm of the bladder.

Course.—Two months after admission the patient became torpid and finally stuporous, in which condition he remained until his death, four days later, with uremia.

Report of Autopsy.—Autopsy showed a carcinoma of the bladder with metastases to the lungs and pelvic and tracheobronchial lymph nodes.

Central Nervous System.—The frontal convolutions were greatly atrophied. The anterior horns of the lateral ventricles were extensively dilated. There was pronounced atrophy of the white matter. The striatum, especially the caudate nucleus, was shrunken. Demyelinated plaques were present in the corona radiata of both hemispheres, in the optic radiations and in the right substantia nigra (fig. 5). Histologically the plaques were typical of multiple sclerosis.

Comment.—Because of the patient's age, the late onset of symptoms and the absence of remissions, the neurologic signs were attributed to cerebral arteriosclerosis. At autopsy the central nervous system disclosed a typical picture of multiple sclerosis.

CASE 6.—Onset of symptoms referable to the spinal cord at age of 41. Progressive course, of eleven years' duration.

History.—A. B., a man aged 50, was admitted to the Montefiore Hospital on Dec. 1, 1931, with a history of staggering gait, intermittent cramplike pains in the legs and weakness of the legs, which began in 1922 and pro-

gressed u
crutches.
with occ
episode o
admission

F
tions
the
conv

feces
May
hosp
discl

gressed until he was unable to walk without the aid of crutches. In 1926 there appeared urgency of urination, with occasional incontinence. A year later the first episode of incontinence of feces occurred, and on his admission there was total incontinence of both urine and

Examination.—There were horizontal and vertical nystagmus, a left Horner syndrome, spastic paraplegia, hyperactive reflexes in all extremities, bilateral ankle clonus, absence of abdominal reflexes, a bilateral Babinski sign, impaired vibration and position sensations

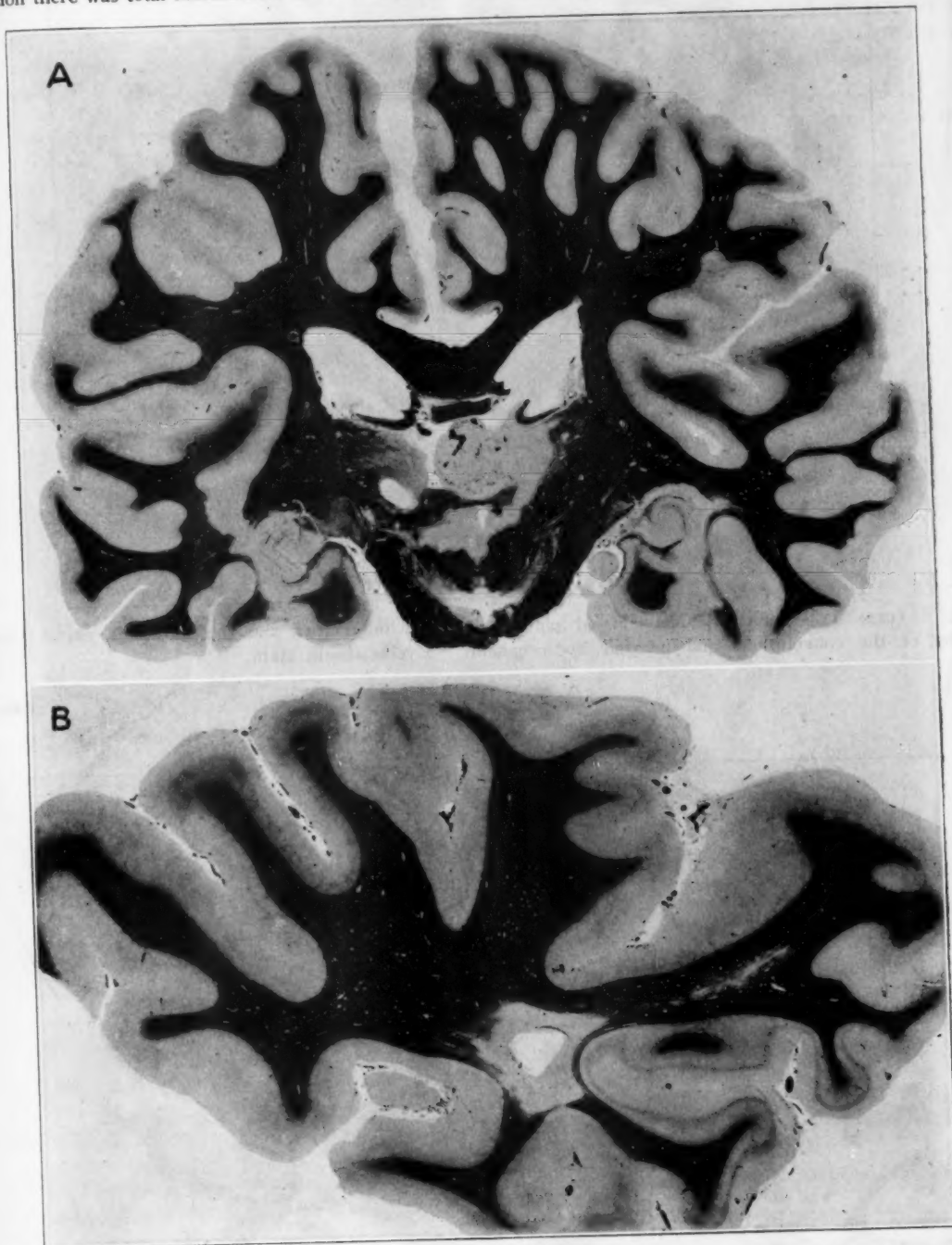


Fig. 4 (case 4).—Areas of demyelination in the white matter of the temporal and hippocampal convolutions, in the thalamic nuclei, about the aqueduct of Sylvius and in the substantia nigra (A), as well as in the white matter around the posterior horn of the lateral ventricle and the white matter of the occipital convolutions (B). Myelin sheath stains.

feces. Loss of power of erection occurred in 1927. In May 1931 a laminectomy was performed at another hospital, but no neoplasm was found and the patient was discharged with the diagnosis of adhesive arachnoiditis.

in the lower extremities and total incontinence of urine and feces.

Laboratory Data.—Examination of the blood and urine revealed nothing significant. The cerebrospinal

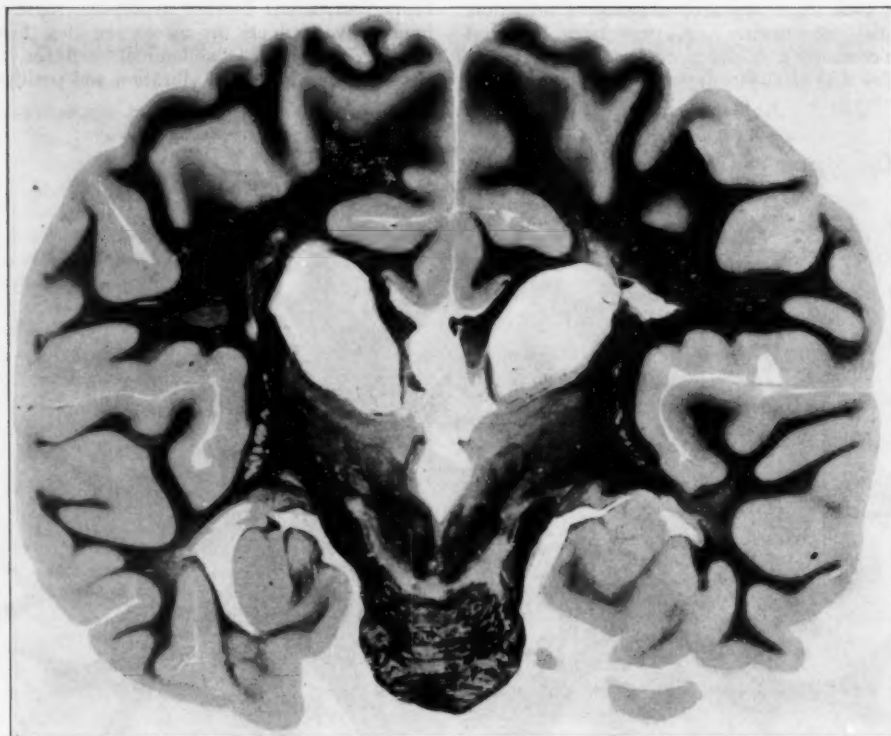


Fig. 5 (case 5).—Numerous demyelinated plaques in the white matter and the substantia nigra. Notice atrophy of the convolutions and internal hydrocephalus. Myelin sheath stain.

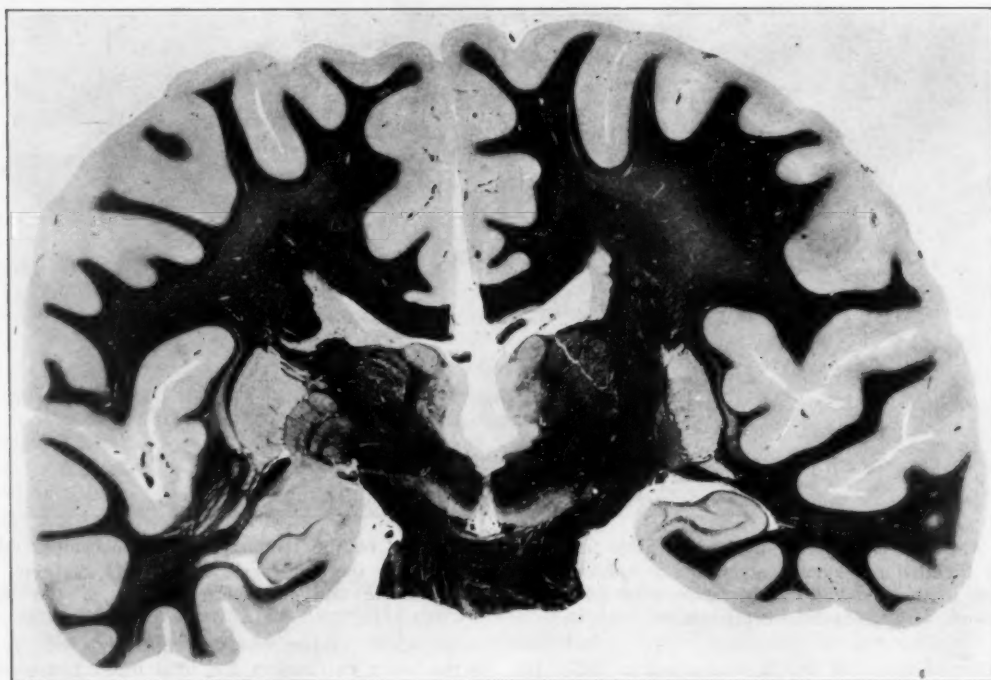


Fig. 6 (case 6).—Small demyelinated area near the ventricle, in the hypothalamus—best seen on the right—and in the insular fibers on the left. Myelin sheath stain.

fluid was
dynamics
The pro
reaction
mal curv

Course
paraplegi
of marke
the patie

Report
slightly

Fi
matter

in the
insula
capsu
denta
cord
show
hypot
cells,
cells
destr
cord
(fig.
not

fluid was under a pressure of 70 mm. of water, and the dynamics were normal. The fluid contained no cells. The protein content was normal; the Wassermann reaction was negative, and the mastic test gave a normal curve.

Course.—Several months after the patient's admission paraplegia in flexion developed. There were periods of marked euphoria. Bronchopneumonia developed, and the patient died in August 1933.

Report of Autopsy.—The frontal convolutions were slightly atrophied. Demyelinated plaques were present

chromatolysis, pyknosis, pigment atrophy and occasional disintegration.

Comment.—Early in the course of the illness the diagnosis of a neoplasm of the spinal cord was made, and an exploratory laminectomy was performed. Later, however, the symptoms disclosed evidences of disseminated lesions.

CASE 7.—Onset of symptoms referable to the spinal cord at age of 40, with diagnosis of tumor of the spinal

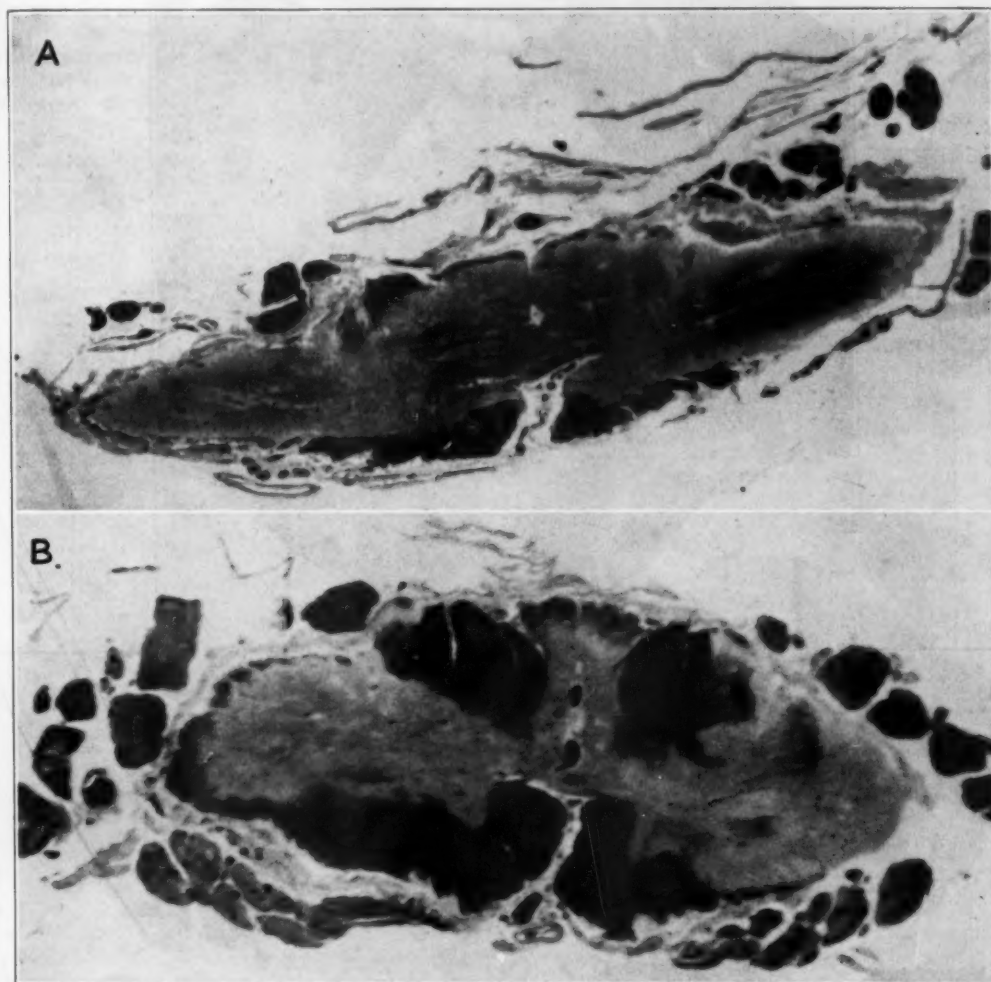


Fig. 7 (case 6).—Demyelinated plaques in the cervical and thoracic regions, with involvement of the gray matter. Myelin sheath stain.

in the white matter of both frontal convolutions, in the insula, near the ventricles (fig. 6), and in the internal capsule, the hypothalamus, the optic radiations, the dentate nuclei, the medulla oblongata and the spinal cord (fig. 7). The myelin sheaths and axis-cylinders showed the changes typical of multiple sclerosis. The hypothalamic region was densely infiltrated with glia cells, especially microglia cells. Some of the nerve cells had a shadow-like appearance, were completely destroyed or showed pigment atrophy. In the spinal cord some of the plaques also invaded the gray matter (fig. 7). The ganglion cells in these areas, although not destroyed, showed pathologic changes such as

cord and laminectomy. Progressive course of two years' duration.

History.—M. S., a man aged 42, was admitted to the Montefiore Hospital on Aug. 8, 1942, with a history of numbness of the hands and generalized weakness since 1940. Shortly after the onset of these symptoms the muscles of the left hand became atrophied. In 1941 iodized poppyseed oil was injected intrathecally. After this, he had difficulty with his gait and complained of severe headaches. Progressive weakness of the lower extremities, difficulty in starting the urinary stream and constipation developed. Four months before his admission a spinal tap was done at another hospital. Within

a few hours after this the temperature rose, and he grew drowsy and became paralyzed from the waist down. Sensation was lost in the lower extremities, and occasionally painful flexor spasms occurred. The

symptoms, a laminectomy was performed, but no tumor was found. On admission to the Montefiore Hospital the patient appeared wasted and malnourished. There were decubitus ulcers over the sacrum.

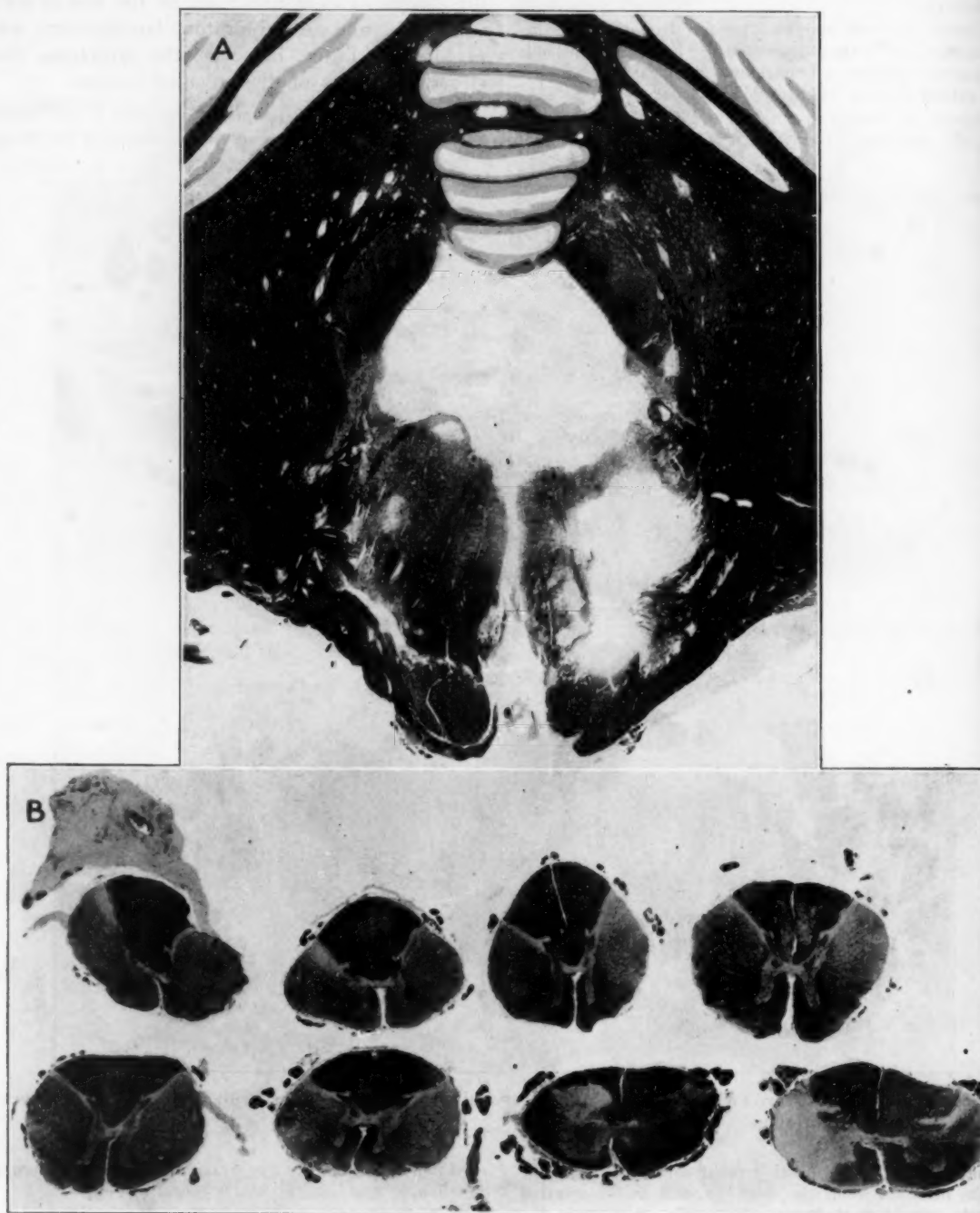


Fig. 8 (case 7).—Demyelinated plaque in the right portion of the brain stem, involving the nuclei of the sixth and the seventh cranial nerves, the trapezoid body, the superior olive, the thalamo-olivary tract, the medial lemniscus and the pyramid (A) and the area of demyelination in the ventrolateral tracts of the thoracic regions and a plaque in the lumbar enlargement (B). Myelin sheath stain.

fluid obtained at this puncture contained 12 lymphocytes per cubic millimeter and a total protein of 75 mg. per hundred cubic centimeters, but there was no evidence of spinal block. Because of the rapid progression of

Examination.—There were horizontal nystagmus, generalized wasting of the musculature, more marked in the distal parts of the arms, hyperactive reflexes in the upper and absence of reflexes in the lower

extremities
examina
ability o

Labor
was not
seconda

Cours
sharp
weeks
monia.

Repor
surroun
Sylvius
nucleus
volved
the fift
seventh

Fi

involv
the th
pyram
nume
nation
lumba
showe
pictur

Ca
atroph
of th
tumo
lesio

CA
age o

extremities and absence of abdominal reflexes. Sensory examination was unsatisfactory because of the unreliability of the patient's responses.

Laboratory Data.—A lumbar puncture at this hospital was not done. Examination of the blood revealed severe secondary anemia.

Course.—The patient was febrile and complained of sharp pain in both upper extremities. He died two weeks after entry to this hospital, after bronchopneumonia.

Report of Autopsy.—There were demyelinated plaques surrounding the superior part of the aqueduct of Sylvius and in the white matter about the dentate nucleus. In the brain stem, a demyelinated plaque involved the posterior longitudinal bundle, the nuclei of the fifth and sixth cranial nerves and the genu of the seventh nerve. In the same area, another large plaque

History.—E. K., a woman aged 52, was admitted to the Montefiore Hospital on May 31, 1942, with a history of severe weakness of the legs in 1936, followed in 1938 by weakness in the arms. Since 1940 the patient had been bedridden. There were also emotional lability and impaired memory for recent events. Six months before her admission urinary incontinence developed.

Examination.—There were horizontal nystagmus, scanning speech, intention tremor, generalized weakness of all extremities, hyperactive reflexes throughout, absence of abdominal reflexes and a bilateral Babinski sign. Sensory modalities were impaired in a diffuse manner, but, because of her mental status, no definite evaluation was given the tests. The patient was euphoric. There were emotional lability, impairment of attention and marked loss of memory for recent events.

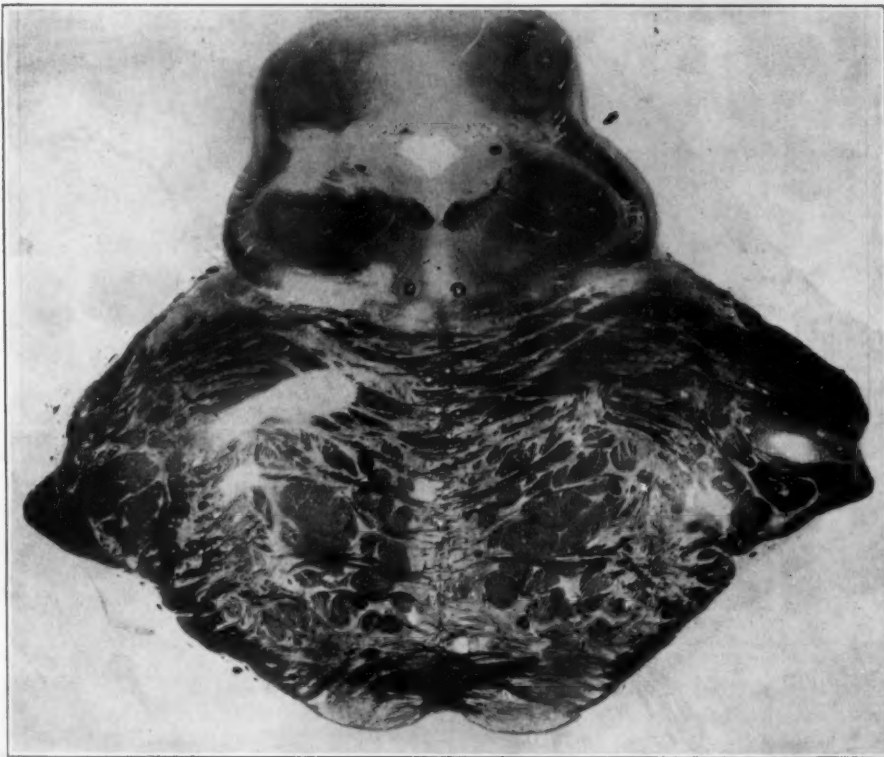


Fig. 9 (case 8).—Numerous demyelinated areas scattered throughout the pons. Myelin sheath stain.

involved parts of the trapezoid body, the superior olive, the thalamo-olivary tract, the medial lemniscus and the pyramid (fig. 8A). Throughout the spinal cord were numerous plaques. The cord disclosed areas of demyelination in the ventrolateral tracts and a plaque in the lumbar region (fig. 8B). The anterior horn cells showed pathologic changes. The rest of the microscopic picture was typical of multiple sclerosis.

Comment.—Because of sensory changes and atrophy of muscles, the diagnosis of neoplasm of the spinal cord was made in this case, but no tumor was found at operation. At autopsy, the lesions observed were those of multiple sclerosis.

CASE 8.—Onset of spinal and cerebral symptoms at age of 46. Progressive course of seven years' duration.

Laboratory Data.—The blood and urine were normal. The Wassermann reactions of the blood and the cerebrospinal fluid were negative. The cerebrospinal fluid was normal except for the total protein content, which was 63 mg. per hundred cubic centimeters. Electroencephalogram and the air encephalogram were normal. A roentgenogram of the chest showed nothing abnormal.

Course.—During her stay in this hospital the patient's condition gradually deteriorated. One year after her admission there developed painless jaundice of obstructive type, due to carcinoma of the pancreas, and she died three weeks later of bronchopneumonia.

Report of Autopsy.—Demyelinated plaques were found in the white matter near the ventricles and in the optic radiations, pons (fig. 9) and medulla oblongata. These were typical of multiple sclerosis. Stains of the spinal cord for myelin sheaths revealed an area of

demyelination in the posterior columns. In the cresyl violet preparations the anterior horn cells, although normal, showed occasional slight pyknosis and shrinkage.

Comment.—Because of the late onset and the absence of remissions, many observers did not consider this case as one of multiple sclerosis.

CASE 9.—Onset of symptoms of the brain stem and spinal cord at age of 43. One remission of symptoms in a course of fifteen years' duration.

History.—C. F., a woman aged 51, was admitted to the Montefiore Hospital on Dec. 25, 1925, with a his-

story of a transitory attack of blindness in the left eye in 1917, followed by numbness of the hands and difficulty in manipulating the fingers. In 1924 there developed weakness of both lower extremities and urinary incontinence.

Laboratory Data.—The blood and urine were normal. The Wassermann reactions of the blood and the cerebrospinal fluid were negative. The cerebrospinal fluid was normal except for a protein content of 56 mg. per hundred cubic centimeters. Roentgenograms of the chest showed some enlargement of the left ventricle and dilatation of the aorta.

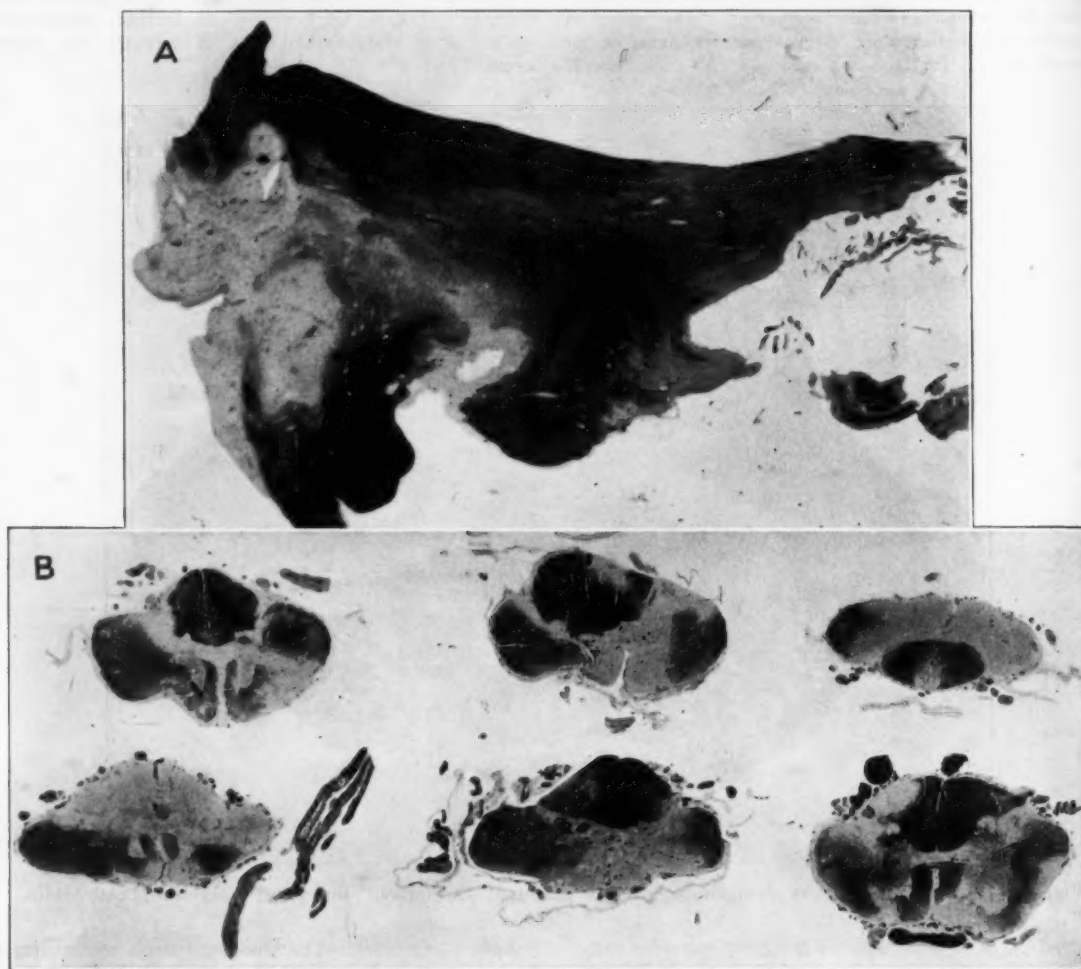


Fig. 10 (case 9).—Plaque in the region of the optic chiasm and tract (A) and numerous plaques scattered throughout the spinal cord (B). Myelin sheath stain.

tory of a transitory attack of blindness in the left eye in 1917, followed by numbness of the hands and difficulty in manipulating the fingers. In 1924 there developed weakness of both lower extremities and urinary incontinence.

She had had influenza in 1918 and an appendectomy in 1921. Arterial hypertension was first noted in 1923.

Examination.—The left pupil was larger than the right but reacted to light and in accommodation. There were pallor of the left optic disk and weakness of the lower right part of the face. The reflexes were hyperactive but equal on the two sides; the abdominal reflexes

Course.—Three months after admission the patient was unable to walk because of weakness of her legs. Examination at this time revealed a sensory level at the seventh dorsal segment. Another examination of the spinal fluid revealed nothing abnormal. In 1927 there appeared horizontal nystagmus, marked memory defect for recent events and emotional lability. In 1928 a diagnosis of diabetes mellitus was made on the results of a routine urinalysis, and the patient was treated with insulin. Weakness and atrophy of the upper extremities became severe. The mental condition deteriorated to the extent that she responded little to questioning, and

these re
There d
had per
and died

Report
frontal
brain sh
nerve
the rig
Sections
elination
The my
changes
slight c
pletely
violet p
with m
multinu
Secti
visible
vascula

Case

1

2

3

4

5

6

7

8

9

tained
areas
destr
flam
glia
large
glia

In
of d
inner
area
calci
comp
Actu
space
cells
The
cereb
lifer
fene
The
An
the
som

these responses were mostly incoherent and irrelevant. There developed severe anemia; she became febrile and had periods of stupor, interspersed with lucid intervals, and died of bronchopneumonia in 1932.

Report of Autopsy.—There was slight atrophy of the frontal convolutions. The vessels at the base of the brain showed atherosclerotic changes. The right optic nerve was shrunken. There were areas of softening in the right putamen. Plaques were not seen grossly. Sections of the optic nerve and chiasm disclosed demyelination of the nerves, tracts and chiasm (fig. 10 A). The myelin sheaths presented all types of pathologic changes, such as complete disappearance, swelling and slight disintegration. The axis-cylinders in the completely demyelinated areas were gone. In the cresyl violet preparations the demyelinated areas were filled with microglia cells, gemästete glia cells and some multinucleated giant cells.

Sections through the substantia nigra showed no visible plaques or areas of softening. A few of the perivascular spaces throughout the diencephalic region con-

tained inflammatory cells. The nerve cells in these areas showed neuronophagia, satellitosis or complete destruction. Occasional glia nodules, consisting of inflammatory cells, microglia cells and a few gemästete glia cells, were also noted. In other regions there were large accumulations of glia nodules, consisting of microglia cells and compound granular corpuscles.

the high cervical region. Areas of discrete demyelination were present throughout. In some regions practically the entire cord was involved (fig. 10 B). The myelin sheaths and axis-cylinders showed changes similar to those in the optic chiasm. In the sudan III preparations lipid deposits were found in the demyelinated plaques; these were more numerous at the border between the completely demyelinated plaques and healthy tissue. In the cresyl violet preparations the demyelinated areas and the gray matter in many sections were filled with numerous glia elements. Some of the nerve cells showed pyknosis or complete destruction.

Comment.—Clinically, this patient presented a picture of multiple sclerosis, which came on at the age of 43. The process essentially involved the optic tract and the spinal cord. Eight years after the original symptoms hypertension developed. Because of this, many observers believed the case to be one of vascular disorder of the

Analysis of Nine Cases of Multiple Sclerosis with Onset of Symptoms After the Age of 40

Case	Age at Onset, Yr.	Duration of Disease	Course	Cause of Death	Signs and Symptoms					Associated Disease	Protein Content of Cerebrospinal Fluid
					Spinal		Brain Stem				
					Tracts	Ventral Horn Cells	Tracts	Nerves or Nuclei	Mental Symptoms		
1	53	2 mo.	1 remission	Postoperative complications	+	—	—	+	—	—	66 mg./100 cc.; increased
2	42	14 yr.	Progressive	Ruptured duodenal ulcer	—	—	+	+	—	Gastric ulcer	Normal
3	41	20 yr.	1 remission	Broncho-pneumonia	+	+	+	+	—	—	Normal
4	43	15 yr.	Progressive	Coronary thrombosis	+	—	+	+	+	Arteriosclerosis, cerebral	58 mg./100 cc.; increased
5	64	1 yr.	Progressive	Uremia	—	—	+	—	+	Carcinoma of bladder	Normal
6	41	11 yr.	Progressive	Broncho-pneumonia	+	—	+	—	+	—	Normal
7	40	2 yr.	Progressive	Broncho-pneumonia	+	+	—	—	+	—	75 mg./100 cc.; increased
8	46	7 yr.	Progressive	Broncho-pneumonia	+	—	+	—	+	Carcinoma of pancreas	63 mg./100 cc.; increased
9	43	15 yr.	1 remission	Broncho-pneumonia	+	—	—	+	+	Diabetes mellitus; cerebral arterio-sclerosis	56 mg./100 cc.; increased

tained inflammatory cells. The nerve cells in these areas showed neuronophagia, satellitosis or complete destruction. Occasional glia nodules, consisting of inflammatory cells, microglia cells and a few gemästete glia cells, were also noted. In other regions there were large accumulations of glia nodules, consisting of microglia cells and compound granular corpuscles.

In sections through the basal ganglia, a small area of destruction was noted between the outer and the inner segment of the globus pallidus. This was a typical area of thrombotic softening. The pallidal vessels were calcified. There was also blood pigment engulfed by compound granular corpuscles and a few glia cells. Actual plaques were not seen. A few perivascular spaces contained lymphocytes, plasma and endothelial cells and microglia cells.

The middle cerebral artery and some of the other cerebral arteries were thickened, and there were proliferation of the intima, splitting of the lamina elastica, fenestration and deposits of cholesterol.

The entire spinal cord appeared thinner than normal. An area of softening was noted at about the level of the seventh and eighth dorsal segments. There was some apparent translucency of the posterior columns in

central nervous system. At autopsy the cerebral vessels and the lesions in the pallidal segments showed changes typical of atherosclerosis. The lesions in the optic pathways and the spinal cord were, however, typical of multiple sclerosis.

COMMENT

Multiple sclerosis is usually considered a disease of young adults, and the diagnosis is rarely considered in cases in which the initial symptoms occur in the fifth or the sixth decade of life. The incorrectness of such a point of view is clearly demonstrated by the present report. In 21 per cent of all cases at the Montefiore Hospital proved by autopsy to be instances of multiple sclerosis, the first symptoms appeared during or after the fifth decade of life (table). Wilson¹ and others have reported similar obser-

vations in series of cases clinically diagnosed as multiple sclerosis.

In our series there were 9 patients with late onset of symptoms (after the age of 40). All were Jewish⁶ and brunette. Five were men and 4 were women. The duration of life after known onset of the disease was from two months to twenty years, with an average of over eight years. The cause of death, as in most cases of multiple sclerosis, was some intercurrent disease, which was bronchopneumonia in 5 patients. Of the other 4 patients the respective causes of death were uremia, coronary thrombosis, perforated duodenal ulcer and a complication following exploratory laminectomy.

The characteristic clinical course of multiple sclerosis is intermittent, with remissions and exacerbations, but occasionally the course may be progressively downhill, without any clear remissions. According to Birley and Dudgeon,⁷ the remittent type occurred six times as frequently in all age groups as the chronic progressive type. In our series the clinical course was progressive in 6 patients and intermittent in 3 patients. Our data support the impression that in patients with the onset of symptoms in the fifth decade of life the disease more often has a chronic progressive course than in those whose first symptoms appear before this period.

The 3 patients whose course was intermittent had the following initial complaints: dizziness, diplopia and pain in the calves. The 6 patients whose course was progressive first complained of numbness and weakness of extremities, disturbance in gait or mental changes. It is possible that the presenting complaints in the patients whose course was intermittent were due to small plaques, while the symptoms of those with a progressive course were the result of larger plaques. Some observers (Putnam⁸ and others) have stated the belief that symptoms due to small lesions tend to regress, while those due to larger lesions are apt to be permanent.

Mental symptoms involving the intellectual and emotional sphere were present in 6 of our patients. Of this group, intellectual deteriora-

tion played a prominent part in the clinical picture of 4 patients.

The diagnosis of multiple sclerosis is unusually difficult when the onset of symptoms occurs after the age of 40 and may be confused with such conditions as neoplasm of the spinal cord, generalized cerebral arteriosclerosis, cerebrospinal syphilis, cerebellar disease, amyotrophic lateral sclerosis, progressive spinal atrophy, syringomyelia, combined system disease and presenile psychosis. In only 2 of our 9 verified cases was the diagnosis of multiple sclerosis made during life, and in both the symptoms developed early in the fifth decade of life and the course was intermittent. In 3 cases an exploratory laminectomy was made because of the predominance of signs referable to the spinal cord with a progressive course. In 1 case the diagnosis was vascular myelopathy; in another, unknown degenerative disease of the nervous system; in a third, olivopontocerebellar atrophy, because of the severe ataxia, and in still another, cerebral arteriosclerosis.

Several factors are important in establishing the diagnosis of multiple sclerosis in the latter years of life: (1) the awareness that multiple sclerosis often begins during or after the fifth decade; (2) more frequent progressive course of the disease; (3) more frequent evidence of loss of intellectual capacities; (4) greater evidence of disease of the anterior horn cells, and (5) a tendency for the signs and symptoms to be more localized, i. e., less clinical evidence of multiple lesions.

SUMMARY

In a series of 310 patients with multiple sclerosis admitted to the Montefiore Hospital, the onset of symptoms after the age of 40 occurred in 41 (13 per cent). Of 42 patients with multiple sclerosis on whom autopsy studies were made at this hospital, 9 (21 per cent) had onset of the disease during or after the fifth decade of life.

The diagnostic criteria of multiple sclerosis in the latter years of life differ from those of the younger age group in the following respects: a tendency to a progressive course, more marked evidence of intellectual deterioration and less evidence of dissemination of lesions. The most important single factor in the diagnosis of multiple sclerosis in the latter years of life is the awareness that the onset of symptoms is not infrequent after the age of 40.

Montefiore Hospital.

6. The exclusive incidence of Jewish patients in this series is due to the fact that the patients admitted to the Montefiore Hospital are predominantly Jewish.

7. Birley, J. L., and Dudgeon, L. S.: Clinical and Experimental Contribution to Pathogenesis of Disseminated Sclerosis, *Brain* **44**:150, 1921.

8. Putnam, T. J.: Multiple Sclerosis and "Encephalomyelitis," *Bull. New York Acad. Med.* **19**:301, 1943.

EPENDYMITIS AND MENINGITIS DUE TO CANDIDA (MONILIA) ALBICANS

REPORT OF A FATAL CASE OF MENINGITIS, WITH COMMENT ON ITS
CLINICAL, BACTERIOLOGIC AND PATHOLOGIC ASPECTS

ARTHUR A. MORRIS, M.D.; G. G. KALZ, M.D., AND E. S. LOTSPEICH, M.D.

MONTREAL, CANADA

Meningeal involvement due to *Candida* (*Monilia*) *albicans* has been described so rarely that the report of a fatal case of meningitis caused by this organism seems justifiable. In the available literature only 2 previously reported cases with definitely established diagnosis were found, 1 by Smith and Sano¹ and 1 by Miale.² It is questionable whether infections of the central nervous system with *Candida albicans* are actually as rare as the literature seems to indicate or whether the condition remains undiagnosed in a considerable number of cases because of the difficulties which the classification of the fungi imperfecti present for the bacteriologic laboratory. The latter point seems to be substantiated by the survey of Freeman,³ in which, besides the well established infections with *Torula histolytica*, *Blastomyces* and *Coccidioides*, cases of meningitis due to "*Endomyces*" and "*Saccharomyces*" with questionable or no bacteriologic studies are cited. The excellent article by Martin, Jones and associates⁴ on the classification of *Candida* should prove of great value to the bacteriologist without any special training in mycology.

REPORT OF CASE

L. S., a 23 year old white Frenchman, complained of dull, intermittent frontal headaches for ten months prior to admission to the hospital. Three months prior to admission he began to notice gradual diminution of vision and diplopia. Two months prior to admission he had a tooth extracted. Shortly afterward he suf-

fered from pain over the vertex, after which his headache became so severe that he was forced to seek hospitalization. Two weeks prior to his admission examination revealed marked vertigo, insomnia, shortness of breath when lying down, constipation for three days, indigestion, progressive amblyopia, scotomas, tremor of the tongue and bilateral papilledema. Three days prior to his admission partial right hemiparesis was noted. Roentgenographic examination of the skull revealed no abnormality; the Wassermann reaction of the blood was negative; the blood sugar measured 88 mg. per hundred cubic centimeters; lumbar puncture revealed a pressure of 550 mm., with 284 lymphocytes per cubic millimeter of fluid. The sugar content of the cerebrospinal fluid was 23 mg. and the protein content 66 mg. per hundred cubic centimeters. Because of the pronounced increase in the cerebrospinal fluid pressure, the patient was transferred to the Montreal Neurological Institute, with the diagnosis neoplasm of the third ventricle.

General physical examination revealed that the patient was well developed but poorly nourished and somewhat emaciated. He complained of severe bifrontal and bitemporal headaches, which were greatly accentuated by any movement of the head or body. There was marked tenderness in the right temporal region to percussion and palpation. There were a moderately diminished light reflex in the right tympanic membrane, a reddened tongue, a slightly reddened and edematous pharynx and loss of a number of the upper and lower teeth. The tongue showed a white exudate from its anterior tip back into, and including, the posterior portion of the pharynx, particularly on the left side. The gums were markedly hypertrophic, especially around the incisor teeth. Mycotic-like lesions were distributed over the chest and trunk, and there was evidence of mycotic infection in the mouth and of mycotic dystrophy of the nails of the ring and index finger of the left hand and the nails of the thumb and little finger of the right hand. Epidermophytosis was present between the toes. The temperature was 100 F., the blood pressure 112 systolic and 70 diastolic, the respiratory rate 20 and the pulse rate 70 per minute. The mental status was difficult to evaluate, owing to poor cooperation and severe temporal and frontal headaches. Bilateral papilledema with hemorrhages and exudates, particularly conspicuous in the right retina, was noted. There was bilateral palsy of the sixth nerve, which was more pronounced on the left side. The patient complained of diplopia on looking to the left, and there was ptosis of the left lid. He lay in bed holding his head to the left side and slightly forward, as this position gave him the least amount of headache. Any change in the position of the head

From the Department of Neurology and Neurosurgery, McGill University and the Montreal Neurological Institute, and the Department of Bacteriology, McGill University.

1. Smith, L. W., and Sano, M. E.: Moniliasis with Meningeal Involvement, *J. Infect. Dis.* **53**:187-196, (Sept.-Oct.) 1933.

2. Miale, J. B.: *Candida Albicans* Infection Confused with Tuberculosis, *Arch. Path.* **35**:427-437 (March) 1943.

3. Freeman, W.: Fungus Infections of the Central Nervous System, *Ann. Int. Med.* **6**:595-607 (Nov.) 1932.

4. Martin, D. S.; Jones, C. P.; Yao, K. F., and Lee, L. E., Jr.: Practical Classification of Monilias, *J. Bact.* **34**:99-129 (July) 1937.

produced severe increase in headache. There were moderate hypertonia, particularly on the right side, and moderate stiffness of the neck. The Kernig and Brudzinski signs were present, and the knee jerks were greatly diminished.

On the night of his admission the temperature returned to normal and his headache subsided. On the second day in the hospital a roentgenogram of the chest showed the left border of the heart shadow to be slightly indistinct, with prominent bronchial-vesicular markings at the bases of both lungs and some accentuation of the root shadows, particularly on the right side. A ventriculogram performed on the second day in the hospital revealed considerable enlargement of both lateral ventricles; the septum pellucidum and the third ventricle were in the midline. There was pronounced enlargement of the third ventricle, and the aqueduct of Sylvius ran slightly farther posterior than might be expected; but the fourth ventricle was visualized, and it did not appear to be displaced. Some of the oxygen had escaped and outlined the interpeduncular cistern. The suggestive block in the neighborhood of the anterior part of the interpeduncular system was typical of meningitis. After the ventriculographic examination the patient's temperature rose to 104 F., and he was placed under treatment with intravenous injections of sulfadiazine. By the following day his temperature had returned to normal, only to rise to 100.5 F. in the late afternoon. Oral administration of sulfadiazine, 1 Gm. every six hours, was maintained for the following thirty-one days. During this time the temperature remained normal. The patient began to moan night and day because of pain behind his eyes and severe headaches. Two courses of potassium iodide therapy failed to give improvement. His headaches then became associated with moderate nausea and occasional bouts of vomiting, and it was suggested that, because of his delirium and increasingly severe headaches, which were not relieved by lumbar puncture, some other type of therapy should be instituted. High voltage roentgen therapy was begun to the base of the skull and administration of the sulfonamide drug discontinued on the thirty-third day in the hospital. He was then maintained on daily high voltage roentgen therapy for the following fourteen days, receiving a total of 2,700 r to the base of the brain and the cervical portion of the cord. No demonstrable improvement could be attributed to the roentgen therapy. He continued to be nauseated, had occasional attacks of nausea and vomiting and took fluids poorly; supplementary intravenous injections were frequently necessary. He continued to complain of headaches in spite of frequent administration of acetylsalicylic acid and acetophenetidin and occasional use of analgesics. After the completion of roentgen therapy, he became restless, complained of severe headache and showed increasing delirium, but the cerebrospinal fluid pressure had returned to below 200 mm. of fluid. Beginning on the fiftieth day in the hospital, he complained of severe toothache and extreme abdominal distention, which was relieved by daily catheterization. At this time he failed to respond to painful stimulation. Four days later, his temperature rose to 106 F., and he died of respiratory failure.

Studies of the cerebrospinal fluid on his admission revealed 29 mg. of proteins, 72 mg. of sugar and 727 mg. of chlorides per hundred cubic centimeters. There were 287 mononuclear cells per cubic millimeter of cerebrospinal fluid, and many round, double refractile bodies were seen on microscopic examination. The

ventricular fluid showed the same double refractile bodies, consistent with the presence of fungus pathogens. Examinations of ventricular fluid for tubercle bacilli gave negative results. Specimens of cerebrospinal fluid and of ventricular fluid were sent to the department of bacteriology for cultural studies and identification. The urine on his admission was normal. Daily lumbar puncture showed a steady increase of protein in the cerebrospinal fluid, ranging from 29 to 222 mg. per hundred cubic centimeters. The sulfadiazine level of the blood during the period of chemotherapy ranged from 6.5 to 13 mg. per hundred cubic centimeters. Daily lumbar puncture during the patient's entire stay in the hospital revealed a pressure between 210 and 750 mm. + of fluid. After the diagnosis of basilar meningitis, daily lumbar puncture, with complete spinal drainage, was carried out, with relief of the severe headaches. The fluid was always bright yellow. The patient complained bitterly of toothache in the right lower jaw. Pus was seen draining from the pocket of the tooth, and cultures of this pus yielded *Candida* (*Monilia*) *albicans*.

BACTERIOLOGIC STUDIES

The yeastlike fungus, which was later identified as *Candida albicans*, was isolated from eight specimens of cerebrospinal fluid intra vitam, from the thrushlike lesions in the patient's mouth, from pus of a draining dental abscess and from the specimens taken at autopsy (exudate at the base of the brain and the abscess of the scalp over the burr hole). The specimen obtained from punctures of the lung (bronchopneumonia of the lower lobe of the left lung) yielded only the usual organisms of the respiratory tract, with large numbers of *Hemophilus influenzae*. The blood cultures were sterile, and no fungi could be isolated from the scrapings of the patient's nails.

The first specimen of cerebrospinal fluid, received on April 4, consisted of approximately 4 cc. of almost clear fluid with a slight yellowish tinge. No pellicle formation was noted. After centrifugation a small amount of a slightly flaky sediment was obtained, adherent to the wall of the tube. No tubercle bacilli were found in stains for acid-fast organisms. Gram's stain of the sediment showed mainly mononuclear cells and some red blood corpuscles. After a prolonged search, a few gram-positive oval and round budding cells were seen. A hanging drop preparation showed a few round and oval budding cells with a vacuole and one or two highly refractile bodies. Only one elongated form, which was thought to be a mycelium, was found.

To exclude any possible contamination, a second specimen was requested, and examination showed the same type of organisms. A preliminary diagnosis of meningitis, due to a yeastlike fungus, was made. The cerebrospinal fluid was planted on blood agar plates. Brewer's meat mash and Sabouraud's agar slants. One set was incubated at 37 C. and one set kept at room temperature. After twenty-four hours the slants at 37 C. showed small, smooth, glistening colonies, creamy white in color. No visible growth appeared at room temperature until forty-eight hours after planting. After forty-eight hours the growth characteristics at 37 C. and those at room temperature were similar. The colonies increased in size but remained smooth. Hanging drop preparations from these young cultures on Sabouraud's solid medium revealed only round and oval budding cells (approximately 5 to 6 microns in

diameter
tile bodi
twenty-f
showed
colonies
a slight
which d
zone, a
revealed
mentary
ment on
weeks'
medium
tics hav
of obser
weeks'
tiation
disting
smooth
type de
in the l
types o
men at
the diff
moistur
was fo
fair am
ment o
to note
diagnos

After
phologi
method
for the
sary m
formul
morpho
strains
those o
dextro
showed
colonie
tion, v
circula
vex, s
carrot
than t
time o
tions
(inocu
dium

Dext
Acid;

'A s
the "i
four c
The
rather
one o
develo
ters o
minal
by in
pletel

Ral
with

diameter) containing a large vacuole and some refractile bodies. The colonies on the blood agar plate after twenty-four hours were small and grayish white and showed the same morphologic characteristics as the colonies on Sabouraud's slants. In Brewer's medium a slight turbidity was noticed after twenty-four hours, which developed into a flaky layer in the intermediate zone, and a wet preparation from a five days' growth revealed the same type of budding cells but some rudimentary mycelial elements as well. Mycelial development on Sabouraud's slants was first noted after three weeks' incubation as fine threads growing into the medium and forming tufts. The cultural characteristics have changed remarkably little in the three months of observation prior to this report. After about four weeks' incubation on Sabouraud's agar slants, differentiation of the colonies into two types could be readily distinguished—one type remained low convex and smooth with a well defined circular outline; the other type developed a honeycomb center, some radial grooves in the border and a slightly lobed margin. These two types of colonies were obtained from the same specimen at room temperature and at 37 C. In our opinion, the differentiation was due entirely to the amount of moisture on the slants, as the former type of colony was found regularly on the slants inoculated with a fair amount of spinal fluid and the latter when sediment only was used as inoculum. It seems important to note this observation, as some authors have attached diagnostic value to the gross appearance of colonies.

After a short observation on the cultural and morphologic characteristics, we followed the valuable method suggested by Martin, Jones and associates⁴ for the final identification of the organism. The necessary mediums were prepared by following exactly the formulas given by the aforementioned authors. The morphologic, cultural and biochemical characters of the strains isolated during the lifetime of the patient and those obtained post mortem were identical. Sabouraud's dextrose acid broth, after forty-eight hours' incubation, showed a heavy sediment but no surface growth. The colonies on blood agar plates, after ten days' incubation, were approximately 1 to 2 mm. in diameter and circular with entire edge and possessed a slightly convex, smooth surface and grayish white color. The carrot plugs have been under observation for more than three months. No asci could be found at any time on repeated examinations. The fermentation reactions were uniform in the special carbohydrate broth (inoculated after three transfers from sugar-free medium and incubated in sealed tubes for ten days).

Dextrose	Saccharose	Lactose	Levulose	Maltose
Acid; gas	Acid	—	Acid; gas	Acid

A stab culture in a corn meal agar tube produced the "inverted pine tree" type of growth in three to four days.

The slide culture technic on corn meal agar proved rather difficult in obtaining uniform results. Only one out of five or six slide cultures showed a well developed "treelike" mycelium, with the ball-like clusters of spores along the hyphal threads and the terminal chlamydospores. The best results were obtained by inoculating the slide before the medium was completely solid.

PATHOGENICITY TESTS

Rabbits.—One rabbit was inoculated intravenously with 1 cc. of a 1 per cent suspension from a twenty-

four hour growth on Sabouraud's medium (Benham⁵). The rabbit died forty-eight hours after inoculation. A summary of the postmortem examination follows. No gross lesions could be found in the lungs, liver or spleen. Careful examination of the heart muscle revealed a few very small abscesses. The kidneys showed extensive abscess formation, mainly in the cortex. These lesions were described as typical of infections with *C. albicans* in rabbits by Benham⁵ and by several other authors. The brain showed a slightly purulent exudate over the entire surface, more prominent at the base. No lesions could be demonstrated in the brain itself. Smith and Sano¹ found abscesses in the brain of the rabbit inoculated with a strain of *C. albicans* isolated from an infant with fatal meningitis and

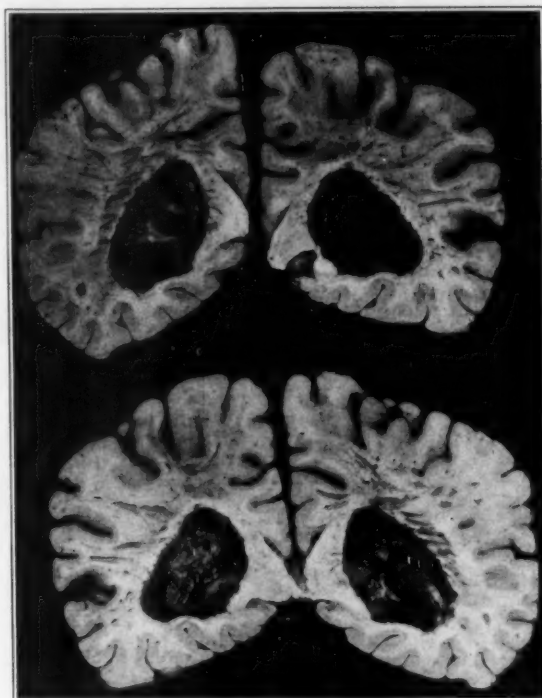


Fig. 1.—Coronal sections of the brain, showing symmetrical enlargement of the ventricles. Large amounts of granular, white exudate cover the ependymal surfaces, particularly the choroid plexus, and bridge the ventricles.

septicemia. We isolated *C. albicans* from the heart blood, the heart muscle, scrapings from the lungs, liver, spleen and kidneys and the exudate of the brain. Direct smears, stained and unstained, of the pus from the abscesses and exudate showed the budding cells and large numbers of mycelial threads. Intracutaneous injections into a rabbit of 0.2 cc. of a 1 per cent suspension caused formation of an abscess in forty-eight hours, from which *C. albicans* was isolated.

Guinea Pigs.—Intraperitoneal injections of 1 cc. of a 1 per cent suspension had no ill effects. The guinea pig is still alive and well, four months after injection.

White Mice.—Intraperitoneal injections of 2 cc. of a 1 per cent suspension had no ill effects. One mouse

5. Benham, R. W.: Certain *Monilia* Parasitic on Man: Their Identification by Morphology and by Agglutination, *J. Infect. Dis.* **49**:183-215 (Sept.) 1931.

was killed two weeks after injection, but no lesions were seen and cultures of material taken from various organs remained sterile. The second mouse was killed ten weeks after inoculation. No lesions were found, and cultures yielded no growth. Four more white mice were given intraperitoneal injections of various amounts of a heavy suspension from a twenty-four hour growth on Sabouraud's medium. One mouse given an injection of 5 cc. intraperitoneally died twenty-four hours later and showed a very pronounced nodular peritonitis, from which *C. albicans* was grown in

of *C. albicans* was not susceptible to penicillin (i. e. in vitro).

PATHOLOGIC OBSERVATIONS

At autopsy the epidural and subdural spaces appeared normal. The brain weighed 1,430 Gm. The subarachnoid space was filled with a grayish white exudate, which extended to involve the base and the upper cervical portion of the spine. Coronal section showed that the ventricles were symmetrically dilated and contained large amounts of granular, grayish white exudate,

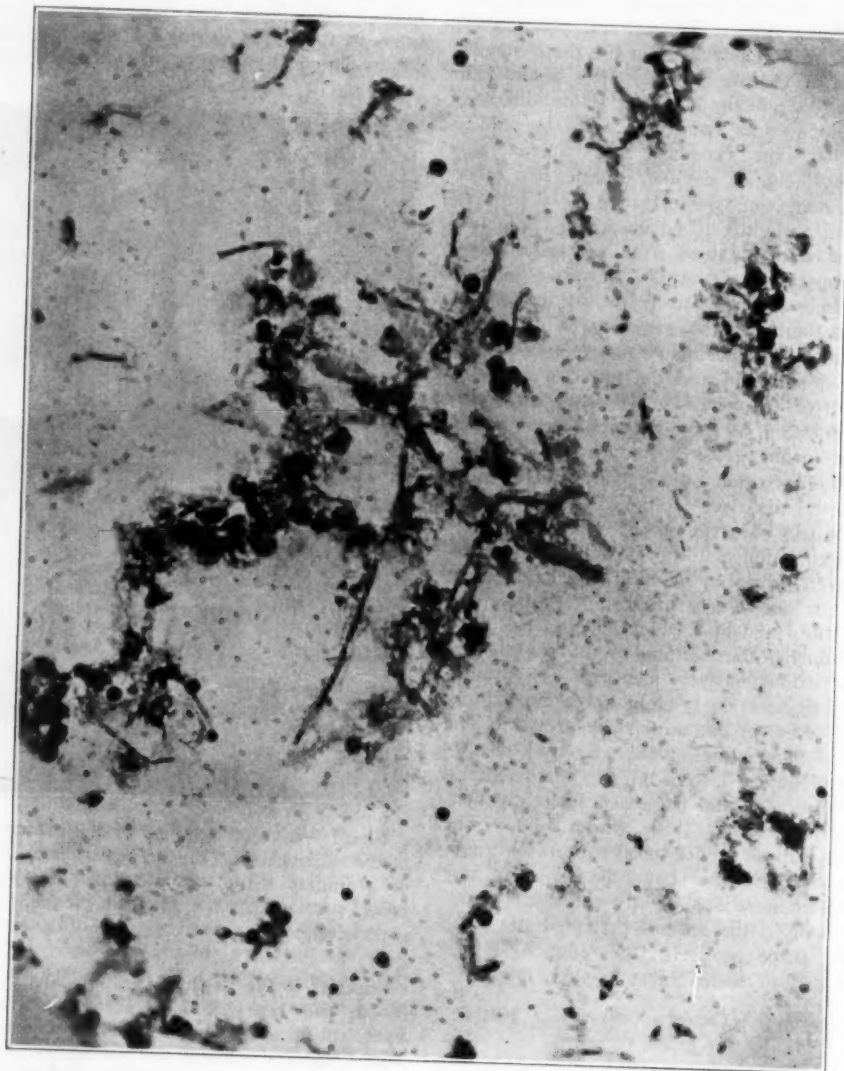


Fig. 2.—Smear taken from the endymal exudate, showing numerous mycelial threads, as well as many round, gram-positive bodies, somewhat larger than lymphocytes.

pure cultures. No growth was obtained from any of the other organs. The 3 other mice died after sixteen to eighteen days. No lesions were found either on macroscopic examination or on histologic study of sections from various organs. No growth was obtained on culture.

Serologic studies were not attempted, since immune serums against the various members of the genus *Candida* are not at our disposal. From the therapeutic standpoint, it was of interest that this strain

covering the endymal surfaces, particularly the choroid plexus, and bridging the ventricle at several places. The exudative reaction was considerably greater within the ventricles than within the subarachnoid space.

Microscopically, the endymal lining had largely disappeared, and an exudate consisting of lymphocytes, necrotic debris and numerous mycelial threads lined the ventricular cavities. Large numbers of multinucleated giant cells were present. Fibrous repair had

taken
of the
and ph
glial nu
had bee
a gran
nucleat
number

A se
showed
lympho
meninge

Com
and S
was gr
subara
small
dymal
as sub

This
of clin
Clinical
tient's
Institut
probab
accura
showed
the ch
the pa
of the
the mo
a cell
meter
tuberc
of the
lumbar
a few
terior
lograph
the pre
vealed
pedunc
of me
routine
were s
histolys
tures t
so that
hands
ment v
quate
of bet
centim
three
the te
Howev
aches,

taken place in some areas. In the adjacent portion of the brain, perivascular infiltration with round cells and phagocytes was seen. There was increase in the glial nuclei. Over certain areas where the ependyma had been replaced the exudate had organized to form a granuloma consisting of large numbers of multinucleated giant cells. Mycelium were seen in large numbers throughout the exudate.

A section through the thoracic portion of the cord showed a minimal amount of exudate, consisting of lymphocytes and some fibrous thickening of the meninges.

Comment.—Unlike the case reported by Smith and Sano,¹ the reactive process quantitatively was greater in the ventricular walls than in the subarachnoid space. Since fibrin, scarring and small granulomas were observed in the ependymal reaction, the process must be considered as subacute or chronic.

GENERAL COMMENT

This case illustrates many interesting features of clinical, pathologic and bacteriologic interest. Clinically, the diagnosis made prior to the patient's admission to the Montreal Neurological Institute was "tumor" of the third ventricle, probably ependymoma. Actually this was an accurate diagnosis, for the pathologic lesions showed "a tumor of fungus" in the areas where the choroid plexus was most extensive. On the patient's admission to the hospital, in view of the positive Kernig and Brudzinski signs and the moderate stiffness of the neck, associated with a cell count of 284 monocytes per cubic millimeter of cerebrospinal fluid, a diagnosis of tuberculous meningitis was made, but because of the severity of the headaches, the danger of lumbar puncture with bilateral papilledema and a few signs of an expanding lesion in the posterior fossa, largely on the right side, a ventriculographic examination was made to determine the presence of the pathologic process. This revealed a block in the upper portion of the interpeduncular cistern, consistent with a diagnosis of meningitis. The organisms were seen on routine examination of the cerebrospinal fluid and were suspected to be either *Blastomyces* or *T. histolytica*. Routine and special bacteriologic cultures then revealed the fungus to be *C. albicans*, so that an accurate clinical diagnosis was in our hands long before the death of the patient. Treatment was apparently of no avail. First an adequate course of sulfadiazine, with a blood level of between 6.5 and 13 mg. per hundred cubic centimeters, was maintained for the first thirty-three days in the hospital, during which time the temperature remained perfectly normal. However, the patient still had symptoms of headaches, nausea and vomiting, and increasing

delirium, increasingly severe toothache and stiffness of the neck, with occasional abdominal distention, diplopia, retro-orbital pain and gradually increasing disorientation, so that some other form of therapy was considered necessary. Then, sulfonamide therapy combined with administration of potassium iodide by mouth was tried over a period from the twentieth to the thirty-fourth day in the hospital, during which time the patient failed to improve. Finally, high voltage roentgen therapy for a period of fourteen consecutive treatments, from the thirty-fourth to the forty-eighth day in the hospital, was apparently without avail. While under roentgen therapy, and immediately after completion of the first treatment, his temperature rose to 102 F. and remained elevated until his death. As far as could be determined clinically, roentgen therapy offered no relief of symptoms in this case.

It was stated by Miale² that mononuclear cells in the cerebrospinal fluid described in his case may have been mycotic pathogens. In the present case, the double refractile, yeastlike organisms were recognized in routine examination of the cerebrospinal fluid and gave a clue as to the cause of the meningitis.

Laboratory studies were not helpful in making the diagnosis prior to the patient's admission, for in a single determination the sugar content of the cerebrospinal fluid was reported as 23 mg. and the protein as 56 mg. per hundred cubic centimeters. The chloride content was not reported prior to his admission. However, on admission the protein of the cerebrospinal fluid measured 29 mg., the sugar 72 mg. and the chlorides 727 mg., per hundred cubic centimeters. In view of the moderate reduction of sugar and the presence of a normal chloride content of the cerebrospinal fluid, tuberculous meningitis seems unlikely. Therefore, in this respect the cerebrospinal fluid did help in making a clinical diagnosis other than that of tuberculous meningitis. The spinal fluid sugar in the case reported by Miale² was always too low to be read, but this was not so in our case, as the sugar in the cerebrospinal fluid ranged from 23 mg. on the patient's admission to 72 mg., per hundred cubic centimeters, on the second day in the hospital.

It is interesting to note that, as in the case reported by Miale,² *Candida* organisms were isolated from the pus of a previously extracted tooth and similar organisms were demonstrated in material obtained from lesions in the pharynx, from exudate over the tongue and from the gums. Whether generalized invasion of the blood stream by mycotic pathogens or direct extension

by way of the cribriform plate was responsible for the meningitis is not known. The fact that Smith and Sano¹ were able to produce focal damage to the brain, as well as meningitis, by the intravenous injection of *Monilia* pathogens into rabbits, previously obtained from a human patient, would seem to support the belief that invasion of the blood stream takes place and that perhaps a special neuropathic strain of *Candida* (*Monilia*) exists. This patient presented rather a mycotic museum, there being obtained evidence of infection with three fungi: (1) *Epidermophyton*, from the feet; (2) *Taenia versicolor*, from the back, and possibly of the finger nails, and (3) *C. albicans*, from the meninges, cerebrospinal fluid, ventricles and brain.

This case is also unique in that the primary diagnosis of cerebral tumor was made in the early stage of the disease. Later, tuberculous meningitis was considered as the most likely possibility. Only until a ventriculogram was made was the diagnosis of meningitis conclusive. Relief of symptoms was at first gained only by repeated lumbar punctures, in an attempt to maintain a normal cerebrospinal fluid pressure. The rapidly accumulating hydrocephalus was due to a block in the interpeduncular system, interrupting the normal circulation over the surface of the brain by way of the subarachnoid space to the longitudinal sinus.

3801 University Street.

An t
the stud
patient
his disc
military
military
two lon
ater of
experie
but th
this di

Fami
Irishma
rhage.
patient
sister
living a
sibling.
ran aw
ried th
times, i
and n
patient'
aggress
sonality
family

Pren
in Mis
where
ures, h
was 10
Mo., v
grocer
driver.
and m
with t
of mu
as a
winter
and M
contra
stone
activit
lent M
he w
presen
pertus
of inf

Pre
at hi
drown
when
him.

NARCOLEPSY

I. COMBAT EXPERIENCE OF A SOLDIER WITH NARCOLEPSY

MAJOR HOWARD D. FABING

MEDICAL CORPS, ARMY OF THE UNITED STATES

An unusual opportunity presented itself for the study of narcolepsy in a combat soldier. This patient began to have symptoms in 1935, and his disorder was not recognized correctly in pre-military life or in the precombat period of his military career. As a result he went through two long campaigns in the Mediterranean Theater of Operations. The unusual nature of his experiences not only provides an interesting story but throws some light on the pathogenesis of this disorder.

REPORT OF A CASE

Family History.—The patient's father, a Scotch-Irishman, died at the age of 64, of cerebral hemorrhage. His mother, aged 69, is living and well. The patient is the sixth of 8 siblings. A brother and a sister died of traumatic causes; the remainder are living and well except for a sister aged 38, the fifth sibling. She is described as being "highstrung"; she ran away from home at the age of 15, has been married three times, remains under a doctor's care at all times, is ill tempered and constantly involves her family and neighbors in useless altercations. From the patient's description, this sister appears to have an aggressive, as well as an inadequate, psychopathic personality. No other neuropsychiatric illness in the family is known to the patient.

Premorbid History.—The patient was born in 1909 in Missouri. After he left school, at the age of 13, where he had completed the sixth grade without failures, he worked on a farm with his father. When he was 16 years old, the family moved to Independence, Mo., where he worked successively as delivery boy, grocery clerk, laborer, foundry worker and truck driver. At the age of 20 he got a job as a gardener and married that year. For the next twelve years, with the exception of one year spent in driving a team of mules on a highway construction job, he continued as a gardener in the summer and a trapper in the winter. During the autumn he traveled through Iowa and Missouri as a corn shucker. He became a sod contractor and employed three men. He learned the stone mason's craft as well. He enjoyed outdoor activities and sports, was a hard worker and had excellent health. His past medical history disclosed that he was never seriously ill before the onset of his present trouble. His only contagious diseases were pertussis, measles and mumps. He gave no history of influenza.

Present Illness.—In 1935 he began to fall asleep at his work while driving a team of mules. He drowsed with the reins in his hands and awakened when his fellow workers on the road job shouted at him. The short attacks of diurnal sleep have con-

tinued since that time. About five months after the onset of the disorder he was hunting with his brother. A rabbit came into view and he raised his gun to shoot; but suddenly his arms and neck began to quiver, and, in his own words, "everything gave way under me and I squatted like a wet rag." Though fully conscious, he remained powerless on the ground for approximately a minute.

After that episode attacks of tonelessness, as well as sleep attacks, were severe. He had to abandon hunting because as a rabbit jumped up he would lose muscular tone and fall to the ground. The noise of the rise of a covey of quail would startle him so that he could not get his gun up into firing position, and when he regained his use of his muscles the quail were well away. He had to abandon the hunting of squirrels because he invariably fell asleep under trees while looking for them. On the other hand, he continued raccoon hunting, watching his dog kill the animals, enjoying the fight but never experiencing a cataplectic attack during these episodes.

He enjoyed boxing but had to give it up because of repeated cataplectic seizures. He stated that he never lost tone as a result of a stinging blow but that "when I got to mixing it up and laughing I'd always go down in a heap." He had to abandon playing baseball as well because he had a cataplectic attack one day in the simple act of trying to catch a pop fly. As is the case with many narcoleptic persons, he avoided raucous laughter as much as he could. He tried not to "feel tickled" at funny stories, avoided pranks and practical jokes on his friends and developed the technic of responding with hollow laughter to humorous situations.

On two occasions he almost drowned during cataplectic attacks. One evening he dived into a small lake, and as he came to the surface he felt an attack coming on. He made one frantic stroke toward the shore but went limp and sank. His brother rescued him, and his muscular tone returned quickly. On a second occasion he was wading in a shallow creek, "hogging" fish. He grasped a large one, which struggled violently as it broke the surface. This exciting display caused a cataplectic attack. He went limp, sank in the water and lost the fish. The timely assistance of a friend kept him from drowning. After these episodes he gave up water sports.

Careful inquiry revealed that pain, anger, shame, grief or worry never caused cataplexy in this patient. Numerous painful accidents while he was working with tools, a painful fracture of a metacarpal bone and a painful head injury did not cause an attack. Angry arguments were never followed by cataplexy. He told of an angry fist-fight which landed both the patient and his adversary in jail, but which was unassociated with any attack. The shame he experienced over this episode and his subsequent trial did not precipitate a seizure. Grief, such as he experienced

at his father's death, and worry over domestic difficulties failed to produce the attacks.

He began to have cataplectic attacks during sexual intercourse within a year of the onset of the disorder. He stated that during the act, just before an orgasm occurred, he would suddenly have a cataplectic attack and go completely limp. These spells would last approximately one minute, during which time penile erection was invariably lost and ejaculation failed to occur. As a result he had to abandon this activity, in which he had formerly taken keen pleasure, and his wife began to run around with other men. He wore the cuckold's horns for more than a year with good grace, but when his wife became pregnant by another man he left her and went to Los Angeles, where he worked in a defense plant until his induction into the Army.

Military History.—He was inducted into the military service on May 3, 1942, at Fort Leavenworth, Kan., and received his basic training at Fort Sill, Okla. He stated that he often fell asleep during "breaks" in the training schedule. His basic training was with the 105 mm. howitzer gun. In July 1942 he was sent to Indiantown Gap, Pa., and was assigned to a field artillery battalion with the rank of private first class. He sailed for Scotland in August 1942. Aboard ship, he was interested in observing gunnery practice, and this occasioned no cataplectic attacks. In Scotland he met a woman and attempted to have sexual relations with her, but a recurrence of his cataplectic attacks during intercourse caused him to abandon this relationship. During the remainder of his precombat training, he had no trouble except for recurrent sleep attacks during training problems. He embarked for the African invasion in October 1942, and on the second day at sea an explanation of the landing operation was given by his commanding officer. The unit was keyed up and eager for combat. There were sharpening of knives and careful inspection of equipment. He looked forward to combat keenly.

African Invasion.—His unit struck the African coast at Blue Beach, near St. Cloud, east of Oran, at about 8 a. m. on November 8. No opposition was met at the landing, and the patient had no symptoms. He saw two dead Arabs, one dead soldier and one wounded soldier. This provoked no attacks. His unit formed itself and marched 5 miles (8 kilometers) inland, then went into an orchard until midnight of the first day, waiting for their guns to come up. The constant rattle of rifle fire from infantry units committed in combat before St. Cloud could be heard ahead of them. The patient stated that as soon as he had dug a foxhole he fell asleep in the hole and slept through the night. In the morning he carried ammunition, and when his job was done, he slipped off and spent most of the day in the foxhole asleep. On the third day the battery moved into a wheat field, where it immediately went into gun position and fired approximately one hundred rounds. His job in the gun crew was that of no. 7, preparing charges of ammunition. He experienced no trouble during his first combat firing mission, even though a shell hit about 75 yards (68.5 meters) behind his battery. After the French capitulation his battery proceeded through the town of St. Cloud, where he saw the scattered corpses of twenty to twenty-five mules and enemy soldiers heaped along the side of the road. He did not respond to these grim sights with cataplexy. He felt after the first days of combat that he could "take it O. K."

His unit moved immediately up into Tunisia, in support of British troops in their attempt to seize the country. The battery was set up in a cemetery below Long Stop Hill. The Germans were in position on the hill, and the tactical mission of his group was to take the hill. They became engaged on Christmas Eve. On Christmas Day his unit was shelled badly. Two members of his battery were killed. He saw them immediately after they were hit. No cataplectic attack developed. The Germans pounded his area severely with 88 mm. shells. The battery commander ordered the men into foxholes. He remained in his foxhole almost the entire day, pinned down by enemy fire. The one road out from their position was under constant shelling. He became extremely jittery and "got the shakes." He became more frightened when infantry units retreated through the area and the realization came that his battery was literally in the front line. Despite this, while in his foxhole, he slept on and off throughout the day. One shell struck about 50 yards (45 meters) away and awakened him. He could hear the cries of his comrades for the "medics," and he knew that some one had been hit. He fell back asleep soon thereafter. Later he was awakened by another soldier, who jumped into his foxhole. After waking he was "plenty scared" and thought his unit would be wiped out entirely. He stated, "I am not much of a hand for prayer, but I thought surely that my end was near that day." On Christmas night the battery disengaged itself and moved back to Medjel-Bab, where it remained dug in for the next six weeks.

During January 1943 he was on a roving gun assignment, which lasted approximately one week. One night during this period his outfit got word that German patrols had penetrated the American infantry. The entire battery was posted for guard duty. Guards were placed approximately 100 feet (30 meters) apart. He was crouched in a foxhole, and at about 9 p. m. he saw a moving shadow. He challenged the man, but the wind was blowing the wrong way and the man did not hear the challenge. The patient followed the shadow and saw the man step behind the shadow of a tree. He jumped out of his foxhole, put a shell into his rifle and threw the bolt. He was about to squeeze his trigger when the other man said, "Don't shoot, Sleepy; it's Jim." At that the patient went into a heap, and his gun fell from his hands. The other man rushed forward to see what was the matter. By the time he had crossed the hundred feet of space between them, the patient had regained his motor power. This cataplectic attack, which occurred when he was about to shoot his friend unwittingly, proved a most upsetting experience, and he remained jittery all night after the episode.

After leaving the Medjel-el-Bab area his battery swung south to the region of the Kasserine Pass. In a flank maneuver, the Germans gained a position of vantage, and the ensuing week was punctuated by great activity; his battery fired approximately four hundred rounds during that time. He states that if he sat down he fell asleep, whether at the gun or at the ammunition pit, 12 feet (3.6 meters) away. During that week of severe combat he often fell asleep between the trails of the gun. It was at this time that he earned the universal nickname of "Sleepy." His fellow G.I.'s often remarked, "I wish I could sleep like you do," or "I don't see how in the hell you can sit down and go to sleep with shells busting all around you."

After the prolonged engagement in the Kasserine Pass area, his unit pressed forward to Gafsa and then on to El Guettar. The men spent the night digging

into position
the German
Just before
a fellow
occurred
reported
area. T
could hear
heart was
throughout
he volun
gully as
gun and
(91 met
for an h
away wa
ahead of
tank ens
out. Du
cataplect
got over
self that
as any p
the Ger
his post
ported l

He w
coming
bomb h
cations
broken.
was su
During
asked
fellow
remain
entire
vacillat
his pos
remain
in one
Polish
to ano
gun b
foxhol
during
sleep
receiv

As
could
destro
"ever
scatte
unit s
from
to st
Whil
(3.6
anoth
him
was
from
to 9
terra
Whil
ing
mid
He
mile
He
tinu

into position, and when morning came they found that the Germans were 300 yards (274 meters) distant. Just before daylight he was given the job of burying a fellow soldier, who had died. No cataplectic attack occurred as a result. When daylight came, it was reported that German tanks were maneuvering in the area. The patient became extremely apprehensive, could hardly stay still and kept moving around. His heart was pounding, and he had a quivering sensation throughout his entire body. While feeling that way, he volunteered to go forward to the mouth of the gully as a lookout. He was armed with a Tommy gun and crawled up forward approximately 100 yards (91 meters) to a place of vantage, where he stayed for an hour. A German tank 500 yards (450 meters) away was shelling a half-track 50 feet (15 meters) ahead of him. A duel between the half-track and the tank ensued. The tank was finally hit and knocked out. During this exciting display he experienced no cataplectic or narcoleptic attack. As he lay there he got over his shakiness; as he stated, "I figured to myself that if I had to get it, I might as well get it here as any place." After that he became calm. He watched the German tanks retreat, and then he went back to his post. He felt "wore out," and as soon as he reported he got into a foxhole and went to sleep.

He was awakened by the bombing of German planes coming directly overhead. A 200 pound (90.7 Kg.) bomb hit within 200 yards (183 meters). Communications between his battery and neighboring units were broken. The battery remained isolated all day and was subjected to dive-bombing throughout the day. During that time he had the jitters very badly. He asked his sergeant what he thought "they'd do to a fellow if he took off and got out of there," but he remained, at his sergeant's advice. Throughout the entire afternoon the patient was extremely jittery, vacillating between fleeing to the rear and remaining at his post. All the members of his unit were ordered to remain in their foxholes, but the patient could not stay in one hole. He said that another soldier, "a little Polish kid," and he "just kept moving from one place to another, from one foxhole to another, to the machine gun bed, to the kitchen, to the battery or back to a foxhole." He said that he was "shaking like a leaf" during the entire afternoon. No cataplectic spells or sleep attacks occurred. During that day his battery received eight attacks by infantry and by tanks.

As evening wore on, it became obvious that the position could not be held any longer. Orders were received to destroy the guns and to retreat. The order called for "every man for himself." In retreat it was necessary to scatter and to climb up over a hill. As the men of the unit scattered fanwise over the face of the hill, shell fire from the enemy rained all about them. The patient had to stop halfway up the hill to rest and catch his breath. While resting, an 88 mm. shell struck about 12 feet (3.6 meters) from him, and he saw shrapnel strike another man in the lower part of the back and wound him severely. The patient thought that surely his time was up. The face of the hill was covered with the fire from 88 mm. guns, machine guns and mortars, as 80 to 90 men were crossing 100 yards of exposed uphill terrain "while enemy stuff was dropping everywhere." While regaining his breath on the side of the hill, watching his entire unit in retreat, and while standing in the midst of the rain of enemy gunfire, he had no attack. He proceeded over the top of the hill and walked 3 miles (4.8 kilometers) back to a concentration area. He fell to the ground and slept immediately and continued to sleep the entire night.

After a period of relative quiet, the unit worked north to a position near Ferryville, where a German railroad gun began to lay down a sweeping fire. The patient was struck in the left shoulder by a piece of spent shrapnel. No cataplectic attack occurred. Later that afternoon an order came to fire five rounds at a particular target. After the first round the gun drew fire from the large railway gun which had shelled them during the morning. The whining of the oncoming shell could be heard long before it hit, and every one on the gun took off and ran to a slit trench 15 feet (4.5 meters) away. The patient had no cataplectic attack during this time. That was the last round of fire by his battery in Africa. Tunis fell later that day, and the campaign was over for his unit.

An estimate of the extent of his sleep attacks can be gained from the fact that one of his buddies appointed himself to the task of looking up the patient at every meal to make sure that he was not sleeping. He said, "I missed a lot of meals by being asleep. The fellows were good about it; and if they weren't too busy with other things, they'd come around and wake me up to get some chow."

After the Tunisian campaign he requested transfer from the gun section to the motor maintenance division, chiefly because in the new position he would not have to stand guard. He never permitted himself to lie down and sleep on guard duty, but he had the uncomfortable experience repeatedly of waking up while standing still or while walking his post. When "pulling" guard duty in pairs, he always insisted on walking the post and having the other man watch, in order to avoid sleeping. His sergeant knew of his affliction and relieved him of guard duty whenever possible, but, despite this consideration, he had averaged one to two hours a night at this duty throughout the campaign. The haunting dread that he might fall asleep on guard, jeopardize his unit and gain himself the death penalty prompted his request for transfer, which was granted.

Sicilian Invasion.—Before the Sicilian invasion the unit cruised along the African coast in an LCT for approximately two weeks. One afternoon the vessel put into a small harbor for water, and his buddies urged the patient to go swimming. On the first dive into the water, as soon as he came to the surface, he knew that a cataplectic attack was coming on. He struck out for a wooden ladder 6 feet (1.8 meters) away, took about two strokes and managed to hook his arm over a rung of the ladder. His head fell limp, and he began to slip into the water. His sergeant swam up to him, asked him what was the matter and helped him gain the ladder. Some seconds later he was able to say, "Nothing is the matter," and he climbed up the ladder and got out.

On the night before the invasion, during a heavy storm, his vessel became lost from its convoy. He was extremely frightened. Waves beat against the vessel and broke over its bow. He stated that he was probably "the scariest one on the boat" and felt that he was surely going to drown. No cataplectic attacks occurred. After midnight the storm subsided, and he fell into deep sleep. He awakened near daylight, when his vessel was off the beach at Gela. There were five or six attempts to get close to the shore, but the vessel ran into shallows. Finally, a pontoon was rigged under the bows of the craft, and vehicles were run out onto the beach over the pontoon. During the laborious attempt to approach the beach, the patient was extremely tense and nervous. A landing craft near his own was hit by an aerial bomb, and the ammunition in its hold exploded violently. A German plane was shot down and landed in the water alongside his vessel. There

was great activity of small boats milling around, and as daylight came he could see the confused combat activity ahead of him on the beach. He was extremely frightened, and he stated that he had a helpless feeling during those anxious hours.

His unit proceeded inland immediately on landing and went into gun position in an almond orchard, about 3 miles from the beach. The Germans surrounded his battery with ten or twelve tanks, and some of them swung around and got between his gun position and the beach. The gun position got a bad raking by German tanks, and the patient had a severe shaking reaction. He could not remain where he was. In an aimless fashion, he wandered away from his battery and went into a vineyard to his left. He stated, "I was terribly scared, and I took off and sort of lost my memory then." He circled around through the vineyard toward the beach. Near the beach he found a haystack. He remained asleep until noon. During that time the air was filled with Naval shells sailing overhead at the enemy tanks. Finally, his battery disengaged itself and retreated to the vicinity of his haystack, where he was discovered and was wakened by his comrades.

The afternoon was quiet; but a paratroop landing in the area began after dark, and this provoked strong action on both sides. The night was filled with rifle and artillery fire. The patient, extremely frightened, could not remain in one place. In the company of his mess sergeant, he started for the beach. They proceeded $\frac{1}{2}$ mile (0.8 kilometer) to the rear, but so many shell fragments from ack-ack guns were falling all about them that they felt it would be safer back at the battery, and they turned around. He fell asleep as soon as he returned to his battery position, although enemy action continued the remainder of the night. His unit recovered its position, then moved through the town of Gela, where there was much firing, and then to a village 8 or 10 miles (12 or 16 kilometers) inland.

Later on in the Sicilian campaign the battery got into position behind a mountain in the Randazzo area. The Germans were shelling a road in the vicinity with six-barreled mortars (*Nebelwerfers*). The missiles from these guns sound like airplanes in a power dive. When the guns opened up, the patient was sitting under a mulberry tree, playing poker. The game broke up quickly; and, in the company of 7 other soldiers, he jumped into a culvert under the road. Rocket mortar shells rained down on them, but he had no cataplectic attacks during the afternoon in the culvert.

During the remainder of the Sicilian campaign the patient, who was in the motor maintenance section, saw little of combat. After the termination of this campaign his unit went to Palma, in the south of Sicily, where they remained four or five weeks in bivouac. He came to England with his unit in November 1943 and remained with his battery for the next two months. One day he went on sick call to request acetylsalicylic acid for a persistent headache, which had begun in Sicily. While waiting his turn the patient fell asleep, and it was then that the medical officer came to the realization that his sleepiness was pathologic and sent him to the hospital. There a diagnosis of narcolepsy was made for the first time, and it was found that he responded favorably to administration of 15 mg. of benzedrine sulfate twice daily. The patient states that after he had been taking benzedrine it was the first time in nine years that he had been able to read a magazine or a book without falling asleep. While in the hospital there, he ran short of benzedrine sulfate tablets and was without them for one day. On the next day he played baseball, and during the game he had a cataplectic attack. As he was going

into position to tag a runner at third base, he felt an attack of cataplexy coming on. He managed to stop the ball with his glove, but he went down in a heap and dropped the ball, and the runner piled on top of him.

Diagnosis.—The clinical diagnosis in this case can hardly be in doubt: The case is one of the narcolepsy-cataplexy syndrome. Physical examination revealed no evidence of a pathologic condition. Neurologic examination failed to disclose any evidence of disease of the central nervous system. The urine was normal; the hemogram was normal, and lumbar puncture released free-flowing, normal cerebrospinal fluid under 100 mm. of pressure. The basal metabolic rate was -4 per cent. Roentgenologic study of the skull revealed nothing abnormal. The absence of clinical, historical or laboratory evidence of preexisting disease of the brain places the case in the idiopathic, or cryptogenic, or undetermined, category. Some features of the case are unusual, but all have been noted before. Attacks of cataplexy at the moment of sexual orgasm were reported by Rothfeld.¹ The narcoleptic victim is sometimes "asleep on his feet" while walking or marching, as was this soldier while walking behind a team of mules or walking a guard post in Tunisia. Such trancelike states have been compared to the cataleptic attacks of the hysterical person. This patient gave no history of "nocturnal paralysis," as Wier Mitchell called it, or "sleep-paralysis" (Wilson), the condition in the crepuscular period between wakefulness and sleep in which the subject is fully conscious but is incapable of moving a muscle. The absence of anger as an excitant of cataplexy is not rare; hearty laughter is the only excitant in some cases. A shaking or nodding of the head at the onset of the attacks of cataplexy, which the patient reported, was first described by Westphal.

COMMENT

The outstanding fact in this case is the paucity of cataplectic attacks during combat. Ample time was available over a series of evenings to review the patient's history minutely, and he was a good witness as well. Careful reflection and repeated review of his combat experience failed to reveal any other attacks than the two cited herein, i.e., the attack when inadvertently he almost shot his buddy and the attack while he was swimming off Bizerte. This is surprising in view of the magnitude of the affective experiences which were heaped on him. The repeated attacks of severe anxiety reactions of the "shakes" variety; a panic reaction on the occasion in Africa when he kept running from one foxhole to another despite orders to lie low, and an amnesic fugue, when he wandered off the battle field to a haystack near Gela, are all evidence of an acute, though abortive, combat neurosis and give testimony to the profound emotional reactions, with consequent disintegration of behavior, that occurred time and again in this soldier.

1. Rothfeld, J.: Ueber Orgasmolepsie und über sexuelle Erregungen bei narkoleptischen Schlafzuständen, nebst Bemerkungen zur Narkolepsiefrage, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **138**:704-719, 1932.

I was surprised that so few cataplectic episodes had occurred, and I told the patient so. He countered with the statement that "being scared doesn't bring those falling spells on. I'm not ashamed to admit that I've been as scared as anybody ever was; and if being scared caused them, the boys would have been picking me up off the ground all the way from Oran to Troina." He went on to point out that it is not a state of fear, or a state of jollity or any emotional state which produces cataplexy, but, rather, that the condition is brought about by a massive stimulus. "It comes on when something big and sudden hits you, when you're not ready for it. Then you're down almost before you have time to have any feeling about it. Big, sudden things

surprise my muscles almost before they surprise me. They've got to be big and fast, though, to knock me down," he insisted.

SUMMARY

The case of a 35 year old soldier suffering from narcolepsy, cataplexy and 'trancelike' cataplectic attacks is reviewed in detail. His disorder began seven years before his induction into the Army; and because it was not recognized he went through two major military campaigns. In combat he lived through many emotion-laden experiences, of a magnitude seldom endured by a patient with this disorder. Despite this, cataplexy was a surprisingly rare occurrence. The case, therefore, casts doubt on the accepted belief that cataplexy results from "emotional" stimuli.

PSYCHOPHARMACOLOGIC STUDY OF SCHIZOPHRENIA AND DEPRESSIONS

II. COMPARISON OF TOLERANCE TO SODIUM AMYTAL AND AMPHETAMINE SULFATE

JACQUES S. GOTTLIEB, M.D.; LIEUTENANT HOWARD KROUSE

IOWA CITY

MEDICAL CORPS, ARMY OF THE UNITED STATES

AND

ARTHUR W. FREIDINGER, M.D.

IOWA CITY

Since the reaction of a psychotic patient to the intravenous injection of sodium amytal has been recognized as being of diagnostic,¹ therapeutic,² prognostic³ and investigative⁴ importance, attempts have been made to improve the response to this drug. Various stimulants of the central nervous system, such as caffeine and sodium benzoate,⁵ metrazol⁶ and amphetamine sulfate,⁷ have been employed for this purpose: to improve the psychologic characteristics of the response, to decrease drowsiness and to prolong the reaction.

From the Iowa State Psychopathic Hospital and the State University of Iowa College of Medicine.

1. Berrington, W. P.: Psycho-Pharmacologic Study of Schizophrenia, with Particular Reference to Mode of Action of Cardiazol, Sodium Amytal and Alcohol in Schizophrenic Stupor, *J. Ment. Sc.* **85**:406 (May) 1939. Sullivan, D. J.: Psychiatric Uses of Intravenous Sodium Amytal, *Am. J. Psychiat.* **99**:411 (Nov.) 1942.

2. Wagner, C. P.: Pharmacological Action of the Barbiturates: Their Use in Neuropsychiatric Conditions, *J. A. M. A.* **101**:1787 (Dec. 2) 1933. Longpre, F.: Sodium Amytal Combined with Psychotherapy in Non-Cooperative and Cataleptic Patients, Massachusetts Department of Mental Health, Symposium on Therapy, September 1939, p. 5.

3. Gottlieb, J. S., and Hope, J. M.: Prognostic Value of Intravenous Administration of Sodium Amytal in Cases of Schizophrenia, *Arch. Neurol. & Psychiat.* **46**:86 (July) 1941.

4. Layman, J. W.: A Quantitative Study of Certain Changes in Schizophrenic Patients Under the Influence of Sodium Amytal, *J. Gen. Psychol.* **22**:67 (Jan.) 1940.

5. Broder, S. B.: Therapy in Catatonia: Effects of Combining Caffeine Sodium Benzoate with Sodium Amytal, *Am. J. Psychiat.* **93**:957 (Jan.) 1937.

6. Reitman, F.: Some Observations on Sodium Amytal Experiments: Preliminary Report, *J. Ment. Sc.* **87**:96 (Jan.) 1941.

7. Myerson, A.: The Reciprocal Pharmacological Effects of Amphetamine (Benzedrine) Sulfate and the Barbiturates, *New England J. Med.* **221**:561 (Oct. 12) 1939. Myerson, A.; Roman, J.; Rinkel, M., and Lesses, M. F.: The Effect of Amphetamine (Benzedrine) Sulfate and Paradrine Hydrobromide on Sodium Amytal Narcosis, *ibid.* **221**:1015 (Dec. 28) 1939.

In a previous study,⁸ the effects of combined intravenous injections of sodium amytal and amphetamine sulfate in patients with schizophrenia and depressions were compared. When a constant dose (sodium amytal, 250 mg.; amphetamine sulfate, 10 mg.) was used and the response of the patient to sodium amytal alone was compared with that to amphetamine sulfate added in different ways on subsequent days, it was apparent that the amphetamine sulfate partially relieved the drowsiness produced by the sodium amytal in both schizophrenic and depressed patients, whereas the psychologic characteristics and the duration of responses differed. For the depressed patients the psychologic characteristics remained unchanged and the duration of the response was increased. For the schizophrenic patients there was a slightly poorer psychologic reaction with no increase in the duration.

The data thus suggested that tolerance⁹ to drugs of the barbiturate series may develop more easily in patients with schizophrenia than in patients with depressions. This hypothesis was further supported by the observed phenomenon that subsequent responses to sodium amytal alone in schizophrenic patients often become poorer—indeed, sometimes they fail to appear at all.³ The present study was therefore designed to answer the question: Do schizophrenic and depressed patients show a similarity or a difference in the development of tolerance to a combination of sodium amytal and amphetamine sulfate?

8. Gottlieb, J. S., and Coburn, F. E.: Psychopharmacologic Study of Schizophrenia and Depressions: Intravenous Administration of Sodium Amytal and Amphetamine Sulfate Separately and in Various Combinations, *Arch. Neurol. & Psychiat.* **51**:260 (March) 1944.

9. The word tolerance as used in this report refers to the psychologic, and not the hypnotic, effects.

METHOD

Twenty consecutive patients who were suitable for testing, 10 of whom had schizophrenia and 10 depressions, were subjected to a routine procedure. Suitability for testing depended on each patient's meeting four requirements: (1) The patient must present typical signs and symptoms of one or the other disorder; (2) he must not have been taking barbiturates for some time before admission; (3) he must not have previously been subjected to any of the shock therapies (insulin, metrazol or electric), (4) and the duration of the initial response to sodium amytal must be measurable by means of clinical observation. Although the last requirement was necessary in planning the procedure, it operated in a selective way on the two patient populations. Of the patients suffering from a depression and meeting the first three requirements, all but 1 had a response to sodium amytal the duration of which was measurable. This was not true for the schizophrenic patients. It required the testing of 22 patients in order to select 10 with suitable responses for the purposes of this study. Actually, then, the comparison was between unselected depressed patients and the better reactors in the schizophrenic group.

On ten consecutive days, after breakfast, each patient was given an intravenous injection of 250 mg. of sodium amytal followed by 20 mg. of amphetamine sulfate. If the type of response became consistently poor and was unmeasurable for three consecutive days, the series of injections was discontinued. The type and duration of the response and the degree of narcosis were noted. The initial drowsiness which occurred on some occasions did not last longer than fifteen to thirty minutes and presented no complication. The duration of the response was determined to the nearest half-hour, its termination being judged by the clinical observation of the patient, that is, when the behavior had returned to the preinjection level.

"The reactions were evaluated as good, moderately good and poor. For the patient with schizophrenia, a good reaction was defined as one in which the affect was warm and appropriate to the thought content, the associations normal and the insight good as far as the patient recognized that he was ill. A moderately good reaction was defined as improvement in affect, associations and insight with persisting evidence of abnormalities. A poor reaction was defined as considerable defect in affect and thinking or as failure to respond.

"For the patient with a depression a good reaction was defined as a shift of the affective state to or nearly to the normal level and, at the same time, disappearance of all evidence of retardation or agitation, whichever was present. A moderately good reaction was one in which there were definite improvement in the affective state and diminution of retardation or agitation but abnormalities were still evident. A poor reaction was characterized by no improvement in any of the symptoms or by complete failure to respond." In some instances the symptoms became more florid but did not seem to shift toward the normal. Symptoms specific to the drug but not to the illness, such as complaints of light-headedness, dizziness, blurring of vision, numbness and weakness of the extremities and signs of ataxia, nystagmus and vertigo, were disregarded.

RESULTS

In table 1 are presented the duration and type of responses elicited by 250 mg. of sodium amytal followed by 20 mg. of amphetamine sulfate in

the 10 schizophrenic patients for ten or less consecutive days. The injections were discontinued after three consecutive poor, unmeasurable, responses. There was a pronounced consistency in both the type and the duration of responses from patient to patient. Each patient, with 1 exception, had his best type of response to the first injection. Each, with 1 exception, had his longest duration of response to the first injection. Each quickly acquired a poor, unmeasurable, response. These poor responses were characterized at the most by varying degrees of drowsiness. Moreover, there occurred a significant correlation between the type and the duration of the responses. There were 3 good responses, with an average duration of three and five-tenths hours; 22 moderately good responses, with an average of two and four-tenths hours, and 55 poor responses, with an average of five-tenths hour. A level of statistical confidence of 0.1 per cent was obtained for the differences between the durations of the moderately good reactions and the durations of the poor reactions on employing the critical ratio technic. This indicated that the durations of the moderately good reactions were significantly longer than the durations of the poor reactions; hence the implication, the better the type of response the longer is its duration.

The means for the durations reflect the consistency of these changes: The mean initial response was three and three-tenths hours and diminished to zero hours by the eighth day.

The changes in both the type and the duration of reaction for the schizophrenic patients become of considerable significance when contrasted with the observations obtained with the depressed patients. In table 2 are presented the duration and the type of responses elicited by 250 mg. of sodium amytal followed by 20 mg. of amphetamine sulfate in the 10 depressed patients for ten consecutive days. The constancy of the type of response may be evaluated by considering each patient separately. It may then be noted that there were two trends. Patients 1, 2, 3 and 6 maintained approximately the same clinical response in terms of behavioral characteristics for the ten consecutive days. The other 6 patients, however, showed day to day variations—patients 8 and 9 relatively little and patients 4, 5, 7 and 10 considerable variability. When the durations of the responses were examined, considerable variability was also apparent, as indicated by the standard deviations for each patient. Patients 1, 3, 6, 7, 9 and 10 had relatively less variability and patients 2, 4, 5 and 8 relatively more. There was a correlation between the type and the dura-

TABLE 1.—Responses of Patients with Schizophrenia for Ten Consecutive Days or Less to Injections of 250 Mg. of Sodium Amytal Followed by Injections of 20 Mg. of Amphetamine Sulfate

Patient No.	Type of Schizophrenia	First Day		Second Day		Third Day		Fourth Day		Fifth Day		Sixth Day		Seventh Day		Eighth Day		Ninth Day		Tenth Day	
		Re- sponse*	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.
1	Undifferentiated.....	G	5	M	4	P	1	P	0	P	1.5	P	0	P	0						
2	Catatonic.....	M	2.5	M	1.5	P	5	P	0	P	0	P	0	P	0						
3	Hebephrenic.....	G	3.5	G	2	M	1.5	M	1.5	P	0.5	P	0	P	0						
4	Catatonic.....	P	3	M	3	M	1.5	P	1	P	0.5	P	0.5	P	0						
5	Hebephrenic.....	M	2	M	1.5	P	1	P	1	P	0.5	P	0.5	P	0						
6	Undifferentiated.....	M	9	M	4	M	5.5	P	1	P	0	P	3	P	4					P	0
7	Paranoid.....	M	2.5	M	3	M	1.5	P	1	P	0	P	1.5	P	0					P	0
8	Catatonic.....	M	1.5	M	1	M	1.5	P	0.5	P	0.5	P	0.5	P	0					P	0
9	Paranoid.....	M	2	M	0.5	P	0	P	0	P	0.5	P	0	P	0					P	0
10	Hebephrenic.....	M	2.5	M	1	M	0.5	P	0.5	P	0	P	0	P	0						
	Mean.....		3.35		2.15		1.85		0.7		0.45		0		P	0		0			0
	Standard deviation.....		2.1		1.3		1.3		0.5		0.2		0.9								1.4

* G indicates a good reaction; M, a moderately good reaction, and P, a poor reaction.

TABLE 2.—Responses of Patients with Pathologic Depressions for Ten Consecutive Days to Injections of 250 Mg. of Sodium Amytal Followed by 20 Mg. of Amphetamine Sulfate

Pa- tient No.	Diag- nosis*	First Day		Second Day		Third Day		Fourth Day		Fifth Day		Sixth Day		Seventh Day		Eighth Day		Ninth Day		Tenth Day		Stan- dard Devi- ation
		Re- sponse†	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	Re- sponse	Dura- tion, Hr.	
1	I. M.	M	4	M	2.5	M	3	M	6.5	M	7	M	3.5	M	5	M	4	M	2	M	7	4.4
2	M. D. M.	G	12	G	6.5	G	8.5	G	5	G	1.5	G	3.5	G	4	G	5.5	G	12	G	3.5	1.7
3	M. D. M.	M	3	M	7	M	5	M	2.5	M	4	M	3	M	2	M	2	M	1	M	1	6.2
4	M. D. D.	G	12	P	6.5	P	2	P	1	M	1	M	1	M	2	M	1.5	M	1	M	1	3.4
5	I. M.	P	12	P	3	M	8	G	7	M	5	P	2	P	2	P	1	P	4.5	P	2.5	3.1
6	M. D. D.	M	2	M	4	M	5.5	M	4.5	M	4	M	3.5	M	3.5	M	4	M	5	M	4.5	5.1
7	M. D. M.	M	8	G	6.5	M	8.5	M	4.5	M	8.5	G	9	G	8.5	M	6	G	5	M	4.5	4.0
8	M. D. M.	G	5	M	2.5	M	5.5	M	5	M	10.5	M	10	M	11.5	M	9	M	8	M	9.5	7.5
9	M. D. D.	M	5	G	2	G	3	M	3.5	M	2.5	M	3.5	M	2.5	M	3	M	2	M	8.5	7.5
10	M. D. D.	P	5	P	1	M	1.5	M	3	M	2	M	2	G	1.5	G	3	G	4.5	G	4.5	2.9
	Mean.....		6.8		4.1		5.9		4.6		4.8		4.4		4.2		3.8		4.5		4.4	2.8
	Standard deviation.....		3.7		2.1		2.4		1.8		3.1		2.7		3.1		2.4		3.2		2.9	1.2

* I. M. indicates involutional melancholia; M. D. D., manic-depressive psychosis, depressive type, and M. D. M. (manic-depressive psychosis, mixed (agitated depressive) type).
† G indicates a good reaction; M, a moderately good reaction, and P, a poor reaction.

COMMENT

10. The failure to differentiate between the durations of the moderately good and the durations of the poor responses would indicate that our scale for evaluating the reactions in patients with depressions was accurate bidimensionally rather than tridimensionally. Further support was obtained by the 86 per cent consistency between the evaluations of the types of responses at the time of injection of the drugs and a reevaluation obtained by reading the descriptions of the individual responses after all the data had been collected. All difficulties in evaluation were between the moderately good and the poor responses. None involved the good responses.

Despite the voluminous investigative work designed to determine the site of action of the

12. Huston, P. E., and Singer, M. M.: Effect of Sodium Amytal and Amphetamine Sulfate on Mental Set in Schizophrenia, *Arch. Neurol. & Psychiat.* **53**: 365 (May) 1945.

barbiturates on the central nervous system, the question is still controversial. Clinically, the narcotizing effect of the barbiturates closely simulates that of physiologic sleep and is interpreted by some observers as evidence of a selective locus of action. In addition, it has been reported not only that patients with chronic encephalitis lethargica show resistance to the drugs but that patients with paralysis agitans show aggravation of their rigidity.¹³ Keeser and Keeser¹⁴ reported deposition of the barbiturates in the thalamus and corpus striatum, none being noted in the pons, cerebellum and medulla. Koppányi, Dille and Krop,¹⁵ however, were unable to confirm this selective distribution of the barbiturates; their data suggested, rather, that these drugs were found in approximately the same concentration throughout the brain. It is well known, however, that the barbiturates antagonize the analeptic effects of ephedrine, amphetamine and picROTOXIN, drugs known to act on the brain stem. In support of this view, Leiter and Grinker,¹⁶ in their studies on the reaction to electrical stimulation of the hypothalamus in cats, found that the responses were more readily elicitable under ether than under dial anesthesia. The present consensus, based on the observations of numerous other investigators,¹⁷ seems to be that the barbiturates act more or less selectively on the hypothalamic functions and by means other than a local action.

Irrespective of the locus of action of barbiturates on the brain, there are a number of observations which when integrated suggest a neural

hypothesis pertinent to the understanding of the psychotic patient. A number of investigators¹⁸ have shown that sodium amytal produces fast frequencies (beta rhythm) outside the normal range in the electrocortical continuum as measured by the electroencephalograph. Moreover, Brazier and Finesinger¹⁹ stated that there is a gradient of response in sensitivity of the electroencephalogram from the frontal to the occipital area. They thus inferred that the regions of the cerebral cortex which are the most recent in phylogenetic development are the most vulnerable to the action of the drug. Rubin, Malamud and Hope²⁰ stated that there is a relationship between the frequency of the electrical potentials and the psychologic changes produced by the drug in schizophrenic patients. Those patients who had a good response to sodium amytal also had considerable increase in the frequency of the electric potentials as seen in the electroencephalogram.

If those observations, then, are integrated with the results herein reported, the problem that presents itself is whether the electroencephalogram will reflect the effect on tolerance to sodium amytal of the two groups of psychotic patients. If these relationships hold true, it would substantiate and allow elaboration of the following hypotheses: There exist a deficient and distorted neural function in schizophrenia and a neural function in pathologic depressions of a different order from that in schizophrenia. These problems are at present under investigation.

Further amplification of these hypotheses of neural dysfunction may be sought in terms of distortion of brain metabolism. Quastel,²¹ in his review, pointed out that the barbituric acid derivatives inhibit the oxidation in vitro by brain tissue of *D*-glucose lactic acid and pyruvic acid. The exact point of action of these inhibitors has not yet been established, but the evidence indicates that the enzyme affected is either a flavo-

13. Goodman, L., and Gilman, A.: *The Pharmacological Basis of Therapeutics*, New York, The Macmillan Company, 1941.

14. Keeser, E., and Keeser, J.: Ueber die Lokalisation des Veronals, der Phenyläthyl- und Diallylbarbitursäure im Gehirn, *Arch. f. exper. Path. u. Pharmacol.* **125**:251 (Sept.) 1927.

15. Koppányi, T.; Dille, J. M., and Krop, S.: Studies on Barbiturates: VIII. Distribution of Barbiturates in the Brain, *J. Pharmacol. & Exper. Therap.* **52**:121 (Oct.) 1934.

16. Leiter, L., and Grinker, R. R.: Role of the Hypothalamus in Regulation of Blood Pressure: Experimental Studies with Observations on Respiration, *Arch. Neurol. & Psychiat.* **31**:54 (Jan.) 1934.

17. Masserman, J. H.: Destruction of Hypothalamus in Cats: Effects on Activity of the Central Nervous System and Its Reaction to Sodium Amytal, *Arch. Neurol. & Psychiat.* **39**:1250 (June) 1938; Effects of Sodium Amytal and Other Drugs on Reactivity of the Hypothalamus of the Cat, *ibid.* **37**:617 (March) 1937. Feitelberg, S.; Pick, E. P., and von Warsberg, A.: Ueber centrale Wärme-Erzeugung und Hemmung durch aromatische Amine und Acetylcholin, *Arch. internat. pharmacodyn. et de therap.* **61**:447 (April 30) 1939. Laidlaw, R. E., and Kennard, M. A.: Effects of Anesthesia on the Blood Supply to the Hypothalamus, *Am. J. Physiol.* **129**:650 (June) 1940.

18. Cohn, R., and Katzenelbogen, S.: Electroencephalographic Changes Induced by Intravenous Sodium Amytal, *Proc. Soc. Exper. Biol. & Med.* **49**:560 (April) 1942. Fowler, O. D.: Neurophysiological and Psychological Changes Induced by Certain Drugs: II. Electrocortical Changes, *J. Exper. Psychol.* **28**:37 (Jan.) 1941.

19. Brazier, M. A. B., and Finesinger, J. E.: Action of Barbiturates on the Cerebral Cortex: Electroencephalographic Studies, *Arch. Neurol. & Psychiat.* **53**:51 (Jan.) 1945.

20. Rubin, M. A.; Malamud, W., and Hope, J. W.: The Electroencephalogram and Psychopathological Manifestations in Schizophrenia as Influenced by Drugs, *Psychosom. Med.* **4**:355 (Oct.) 1942.

21. Quastel, J. H.: Respiration in the Central Nervous System, *Physiol. Rev.* **19**:135 (April) 1939.

protein, functioning as a link between dehydrogenase and cytochrome, or an unknown component of the cytochrome system. It is suggested that the effect of the narcotic is to diminish the ability of the nerve cells to oxidize pyruvic acid, lactic acid and *d*-glucose. The access or activation of oxygen is unimpaired, as shown by the lack of effect of the narcotic on the oxygenation of sodium succinate or *p*-phenylenediamine.

Since the schizophrenic patient so quickly loses his ability to respond psychologically to repeated injections of sodium amytal, the question arises whether there may not be some pre-existing disturbance of the neural metabolism which would be involved in the aforescribed narcotizing process. The injection of sodium amytal, then, would put additional stress on an already faulty mechanism—hence the responsiveness of the organism would be inadequate.

SUMMARY

Sodium amytal followed by amphetamine sulfate was administered intravenously on ten consecutive days to 10 patients with schizophrenia and to 10 patients with pathologic depressions.

1. Whereas 10 of 11 depressed patients had reactions that could be evaluated clinically, it required the examination of 22 schizophrenic patients to obtain 10 with initial responses sufficient for clinical evaluation.

2. For the 10 schizophrenic patients, each, with 1 exception, had his best type and longest duration of response to the initial injection of the drugs. The responses rapidly diminished

and became clinically unmeasurable by or before the eighth day. A statistically significant correlation was obtained between the types and the durations of the responses: The better the type of response, the longer was its duration.

3. For the 10 depressed patients, there was considerable intraindividual, as well as inter-individual, variability in both the type and the duration of response throughout the ten day period; however, the average of the durations remained fairly constant from the second through the tenth day. A statistically significant correlation was obtained between the types and the durations of the responses: The better the type of response, the longer was its duration.

CONCLUSIONS

Patients with schizophrenia are characterized by reacting to the intravenous administration of subnarcotic doses of sodium amytal and amphetamine sulfate with (a) psychologic responses which, in the present study, were clinically measurable in approximately 50 per cent of the group and (b) the rapid development of tolerance in terms of type and duration of the psychologic responses. In contrast, patients with pathologic depressions are characterized by reacting to the same drugs with (a) psychologic responses which, in the present study, were clinically measurable in approximately 90 per cent of the group and (b) absence of rapid development of tolerance in terms of type and duration of the psychologic responses.

Iowa State Psychopathic Hospital.

LOCALIZING VALUE OF VERTICAL NYSTAGMUS

LIEUTENANT COMMANDER F. H. O'BRIEN (MC), U.S.N.R.

AND

COMMANDER M. B. BENDER, MC(S), U.S.N.R.

Vertical nystagmus has been considered a sign of disease in the upper portion of the brain stem, the midbrain or the pons. Thus, Stengel,¹ in 1935, reported a case of vertical nystagmus in which autopsy revealed an area of softening in the caudal part of the pons. Marburg² stated that vertical nystagmus was clinically observed in cases presenting lesions in the region of the colliculi, and Leidler³ was able experimentally to produce the same phenomenon with lesions in the cranial portion of the vestibular nuclei of rabbits. Spiegel and Scala,⁴ working with cats, brought about vertical nystagmus with lesions in the cerebellar vermis. There has recently come under our observation a case in which vertical nystagmus occurred after occlusion of the anterior spinal artery of the medulla.

REPORT OF A CASE

A 52 year old chief yeoman, U.S.N.R., was admitted to the hospital with the presenting complaint of increasing weakness of his right arm and leg for about one month. During the same time he had experienced some difficulty in speaking and swallowing. About four days before his admission to the hospital, he had been troubled with pain in his chest and a cough productive of rusty sputum and thick mucus.

He appeared to be acutely ill but, although somewhat stuporous, could be aroused, when he responded clearly to questioning.

Neurologic examination revealed flaccid paralysis of the right arm and leg and evident weakness of the opposite

From the United States Naval Hospital, San Diego, Calif.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

1. Stengel, E.: Zur Frage der Herdlokalisation bei spontanem Vertikalnystagmus, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **153**:417-424, 1935.

2. Marburg, O.: Modern Views Regarding the Anatomy and Physiology of the Vestibular Tracts, *Laryngoscope* **49**:631-651, 1939.

3. Leidler, R.: Experimentelle Untersuchungen über das Endigungsgebiet des Nervus vestibularis, *Arb. a. d. neurol. Inst. a. d. Wien. Univ.* **21**:151-212, 1914.

4. Spiegel, E. A., and Scala, N. P.: Vertical Nystagmus Following Lesions of the Cerebellar Vermis, *Arch. Opth.* **26**:661-669 (Oct.) 1941.

extremities. The tendon reflexes on the right side were more pronounced than those on the left. The superficial abdominal reflexes could not be elicited. There was a classic Babinski toe sign on the right, and the left plantar response betrayed extensor elements. There was no facial weakness.

Perception of pinprick and cotton stimuli was diminished on the right side except on the upper part of the face, but including the right side of the chin. The patient failed to recognize common test objects in the right hand and identified them poorly in the left. Position sense was greatly impaired in the fingers and toes on the right side and was only slightly less defective in the toes of the left foot.

The usual point to point tests were inaccurately executed with the left hand, although rapid, rhythmic, alternating movements were fairly well performed.

The eyegrounds were not remarkable. The pupils had, unfortunately, been dilated by the instillation of a mydriatic. The extraocular movements were unimpaired. There was rapid nystagmus in all directions of gaze, specifically on looking to the right and the left and upward and downward.

The palate rose promptly in the midline, and the gag reflex was elicited from both sides of the pharynx. Swallowing was performed against resistance. The sternocleidomastoid and trapezius muscles appeared equally strong on the two sides. The tongue was directed forward on protrusion.

Two days later the patient was found to present paralysis of the left side as well as the right, again except for the face. Both plantar reflexes were of Babinski type.

Sensation was difficult to evaluate, but vibratory sensibility appeared to be lost except over both clavicles.

The tongue curled to the left when protruded.

Nystagmus was now present on horizontal gaze, the right component being stronger than the left. Depression of gaze, though well performed in range, was poorly maintained.

The spinal fluid was normal. The Kahn reaction of the blood was negative. The patient died on the sixth day in the hospital, having presented the typical signs of bronchopneumonia.

Autopsy revealed an area of gross softening in the region of the medulla at the level of the inferior olives and the presence of thrombosis of the anterior spinal artery of the medulla.

Microscopically, the damage was most evident at the same level, involving the pyramids and the medial fillets, and to some extent the posterior longitudinal bundle on the side on which the destruction was more apparent (figure).

The series of events following occlusion of the anterior spinal artery of the medulla has been

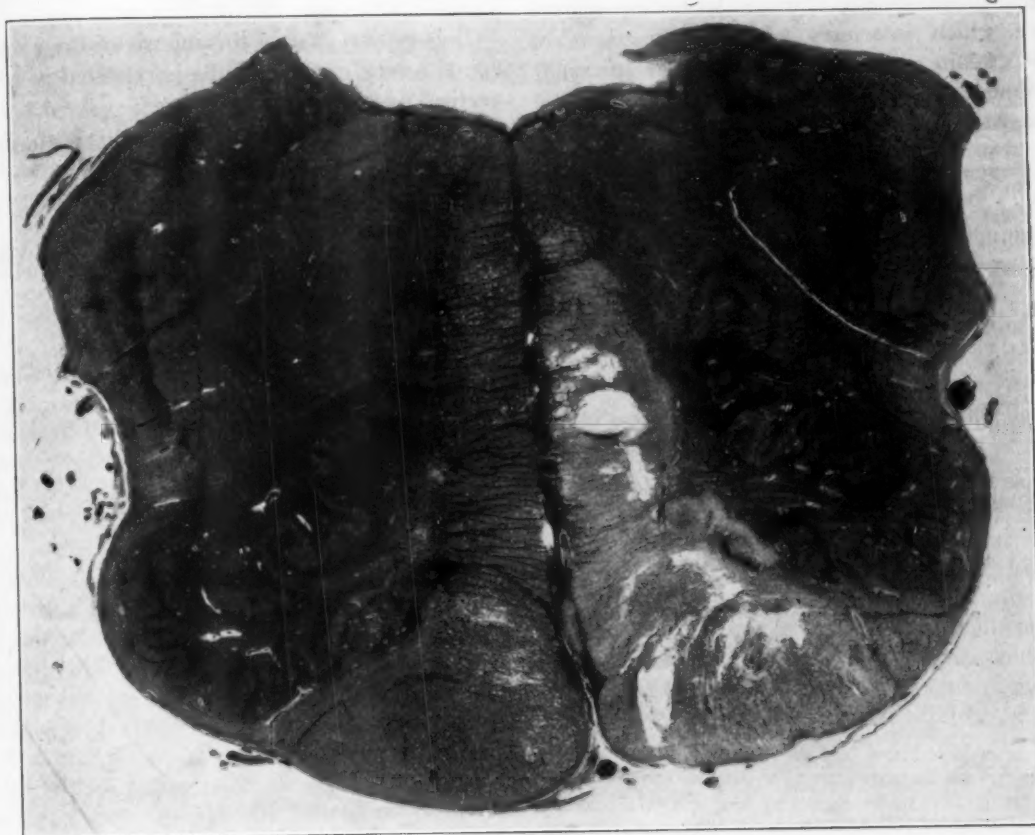
emphasized by Davison.⁵ As he reported, the lesion is not common, occurring in only 4 of his series of 700 cases of cerebrovascular disease verified at autopsy.

Briefly, the syndrome of occlusion of the anterior spinal artery of the medulla consists in signs and symptoms indicative of loss of function of the pyramidal tract and the posterior column, usually below the head on the side opposite the lesion, and occasionally ipsilateral paralysis of the tongue. Davison noted that in the presence of only one anterior spinal artery, both

sented clinicopathologic examples of disease in the medulla producing transient nystagmus in the vertical plane.

COMMENT

Evidently, vertical nystagmus may follow on lesions at various levels of the brain stem. Per se the sign cannot be considered indicative of a defect in the midbrain, the pons or the medulla. Its only importance as a clinical sign is its general indication of disease of the brain stem. Leidler³ attempted to establish direct correlation



Horizontal section of the medulla, showing maximal destruction on the left (at right of photograph), with involvement of the pyramids and the medial lemnisci (distribution of the medullary portion of the anterior spinal artery).

pyramids and medial lemnisci might be involved, producing sensory and motor loss on both sides. He also reported nystagmus in at least 1 of his cases, stating in effect that in addition to coarse horizontal nystagmus there was variable nystagmus on upward gaze. Thus, here are pre-

of vertical nystagmus with lesions in the region of the vestibular nuclei above the level of the abducens nucleus in the rabbit. By producing lesions in the area of the arcuate fibers of the ventrocaudal portion of Deiters' nucleus at the level of the genu of the facial nerve, he obtained horizontal and/or rotatory nystagmus.

This direct relationship of vertical nystagmus to a specific level does not seem to apply either in man or in all experimental animals, for one of us (M. B. B.) has observed in monkeys move-

5. Davison, C.: Syndrome of the Anterior Spinal Artery of the Medulla Oblongata, *Arch. Neurol. & Psychiat.* **37**:91-107 (Jan.) 1937; Syndrome of the Anterior Spinal Artery of the Medulla Oblongata, *J. Neuropath. & Exper. Neurol.* **3**:73-80, 1944.

ments of the eyes in the vertical plane produced by stimulation of structures within and immediately ventral to the medial longitudinal fasciculus, even at the level of the hypoglossal nucleus. Moreover, transient upward and downward nystagmus occurred after damage in the same area.⁶

The fact that vertical nystagmus may be seen after lesions at different levels of the brain stem is readily explainable in terms of Lorente de Nó's⁷ concept of the vestibulo-ocular system. He pointed out the existence of numerous inter-related neuronal circuits of widespread existence in the brain stem. Thus, a lesion or disturbance which interferes with the functions of these circuits may produce a disorder in ocular movements, such as nystagmus. The type of nystagmus so produced, rotatory, horizontal or

vertical, does not depend entirely on the site of the structural defect but is determined by the altered function of the neuronal chain involved.

It is well known that the diagnosis of localization in the brain stem, or indeed of localization anywhere in the nervous system, must ultimately be made by utilization of all the signs present in a given instance. In the case at hand, vertical nystagmus was but one of many signs, and the least significant of all. The neighborhood signs established the level and strongly suggested the nature of the lesion.

SUMMARY

1. A typical case of thrombosis of the anterior spinal artery of the medulla is reported in which vertical nystagmus was observed.

2. The localizing value of vertical nystagmus is briefly discussed.

3. It is concluded that vertical nystagmus *per se* is of little localizing value except in so far as clinical experience has shown it to be sometimes seen in cases of disease of the brain stem.

6. These experiments, as yet unpublished, were carried out with the Horsley-Clarke apparatus in collaboration with Capt. E. A. Weinstein, Medical Corps, Army of the United States.

7. Lorente de Nó, R.: The Vestibulo-Ocular Reflex. *Arc. Arch. Neurol. & Psychiat.* **30**:245-291 (Aug.) 1933.

EMOTIONAL TRAUMA RESULTING FROM ILLEGITIMATE BIRTH

NANDOR FODOR, LL.D.

NEW YORK

For the normal development of a child, the presence of each parent is equally necessary. No man searches more passionately for a dream woman than the child who grows up motherless. The mother is the foundation stone of the world for the infant. A stepmother, nurse or orphanage care never fills the gap which the absence of the mother leaves. However exemplary the manner in which the child's needs are cared for, foster parents and institutions cannot enter into the same psychic bond which the prenatal community of life and immediate postnatal maternal care establish.

While the need for the mother is peremptory and immediate, the father does not enter the child's life until consciousness develops sufficiently for the meaning of home and family to be grasped. When this stage is reached, the absence of the father or suitable father substitutes leaves the child without an important balancing influence. The male parent should be a pillar of strength and a hero ideal for children of both sexes. He should be a god in the infant's universe. His twilight will assuredly come; it is right that it should. But if by brutality the eidolon is shattered prematurely by the father himself, the child's character development may be warped by hatred and fear of the strong parent, and seeds of neurosis may be sown, with the promise of an unwholesome harvest. A boy whose father is cruel may run away from home too soon and vent his hatred on the social order by becoming a criminal or a revolutionary. A girl may develop a masculine character because she has to lean on herself; she may not marry for fear of finding the father duplicated in her husband, and she may be driven to her own sex for the satisfaction of her love needs.

A similar situation to that created by the absence or failure of the parents results from the feeling of not being wanted. The parent who inspires this feeling in the child is guilty of nothing short of a crime. In the world of grown-ups the child is at a natural disadvantage and far too open to adverse suggestions. Because life can be overwhelming, every child needs constant assurance of its own goodness and wel-

come, or self rejection will follow. The child who has failed to accept itself will grow up with a crippling feeling of inadequacy or, if the environment is conducive to the development of an aggressive character, in open rebellion against society.

In the case of illegitimate birth the child's reactions to life are bound to be completely abnormal. It happens but very seldom that children are left unaware of the stain on the family escutcheon which their very life represents. To be fatherless is hard enough, but to be fatherless with the stigma of illegitimate birth is a psychic catastrophe. It is one of the iniquities of our Western culture that a man may morally fail his child with impunity and that instead of the father we punish the child. It would be far more logical to make the father a social outcast than the child, if we must have a conception of illegitimacy.

A MODERN LUCIFER

For an abnormal development it is not necessary that the child should be actually illegitimate. The imputation of such illegitimacy produces equally severe psychic scars. I shall illustrate it with leaves from the life of a 40 year old man who came to me for help seven and a half months after a violent attack of schizophrenia.

Ever since the attack he had heard subjective voices from various isolated compartments of his unconscious mind. These voices produced much mental confusion but also answered questions and told surprising stories of their relationship to the total personality.

The patient's dream life appeared to be more or less independent of their influence. The voices developed so much interest in psychoanalysis that the effect often was as if there were several patients on the analytic couch instead of one. They listened with avid interest to the dream revelations and to the interpretation of the symbols used, often trying their own hand at the art.

One day the voices reported that an important message had come through in the patient's dream. This is how they worded it:

"Your mother says you were not wanted. You were brought into this world because she could not help it. You were more trouble to your father and to your mother than you were worth. It is not alone that you were sick at birth and thereafter. Your father thought that some one else had been with your mother. He used to scream at her: 'I would like to kill that s—

of a b—who slept with you while I was working in the fields to keep the house going.’”

Later, the voices quoted another statement of his father:

“That d—bastard should have died before he was born. . . . I will kill that bastard yet.”

The accusation was untrue. The patient grew up in his father's likeness and with many of his character traits. From the age of 4 he was accepted by the father as his legitimate son.

However, the damage was done. Added to it was the fact that because of the father's hostility, and perhaps for many other reasons, the mother's resentment against him was even more serious. The voices claimed that they were aware of her hostility from earliest childhood and that the patient's suicidal compulsion developed under the effect of the mother's constant death wishes against him.

Whether the voices quoted from forgotten memory, telepathic perception or fantasy makes little difference. Their statement was evidence that great harm was done to the patient by the failure of both parents, and this harm had the lion's share in his final psychotic outbreak. According to his own account:

“I went out of my head and wrote to my sister that I was crazy. The voices told me that I was and that they were going to kill me. The Devil offered me unlimited power if I would do his bidding. He said he would give me half of hell to rule over when I died. He would under no conditions let me go to heaven because I knew too much about him and would put him out of business. I was supposed to rule the world and wipe out civilization. There was a new force by which the mind of man could be controlled. It came from another planet, and it manifested itself through me.”

Being a bastard (as it was impressed on his infantile mind), he was locked out of the family circle, as Lucifer was cast out of heaven. As Lucifer raged against God and man, so did he, never fully realizing that he wanted to destroy his own father and mother and that God and the world were substitutes on a stupendous scale for the family into which he was born.

The strength of his moral streak kept him from committing homicide, and by a miracle he escaped being locked up. The voices raved and cursed, impelling him to kill his father and mother and his younger brother, Al. He resisted them. By the time he came to me for help, his homicidal mania had died down, but amazing light was shown on it in retrospect by the dialogue that took place between him and the voices when he was on the analytic couch.

“We did not kill father, did we?” the voice said.

“No, he is still alive,” he answered.

“But, Fred, you swore you would kill him!”

“Of course I did, but I was angry then.”

I interrupted: “Did you swear to kill Al, too?”

“Did I?” he asked, and the voice answered:

“Yes, you did, once.”

“I did not swear that, but I did swear to kill my mother.”

“When you swore that, we knew it would not be done. But how could you forgive your father? Can't you remember those things? We have it all here. We hated him.”

“I did, too.”

“But, Fred, don't you want to kill him now?”

“No.”

“We can't understand that. We must give up and realize that those childish things are gone. Fred, we hated him awfully much.”

“Yes, we did; but that does not matter now.”

“Fred, we don't understand. We hate him here because we have not been told how to stop it. Because we hated father, hatred of Al still stays. We transfer it back and forth. When you worked on Al, we transferred it back to father. How could we but keep it alive? Why don't we kill father? We hate him here. We have never given that up. It is only your conscious mind that has forgiven him. Now what do we do? We told you our fantasies, as you call them. They are real here. We hate him, and we swore we would kill him. Why didn't you shoot him when you had a chance? When you were home at Christmas and saw his gun? Why didn't you do it? Don't you see, Fred, we hate him; God damn it, we hate him! When we cannot hate him, we hate you.”

Here was the startling revelation by the inner voice that the hatred of his father, not being allowed a release in a criminal act, turned on him and was destroying the peace of his mind. Now he realized it himself and worded it this way:

“The voices made me my own father. They turned on me to keep the hatred alive.”

“Yes, Fred,” the voice answered. “We kept up this hatred against you because you would not kill father. We were killing you instead. We wanted him to die in pain. We wanted to chop his head off. We wanted to have his guts out. We wanted to burn him, as he burned Al's hands with a match. Do you remember how he screamed? Fred, would not fire have been a good way to kill him?”

The statement explained a lot of fire fantasies that came out in the patient's dreams.

“We wanted to kill father for beating mother. She was fighting him. We wanted to help her, but you were afraid. He kicked her and hit her, and she kicked him back in the crotch. We did what your mother tried, kick him there. We do that, don't we?”

Here was the explanation of a persistent pain in the testes from which the patient had suffered ever since his psychotic dissociation began. He always ascribed it to the voices, explaining that he was tortured by them. For the first time, the story was out. He suffered the way he wanted his father to suffer. But he suffered on a double score, not only because he had criminal fantasies against his father, but because he refused to yield to them—a truly amazing psychic state.

POLITICAL CONVERSION

I shall now show the impact of actual illegitimate birth on the dream life of an English woman who, on her mother's side, came from a noble line. She dreamed:

“A Nazi general was walking down the street. I had just read that all our ships were destroyed in the Channel. It was simply terrible. I called to him and asked him if his name was Nègre. He turned round

politely
newspap
in the L
sleeve a

“Then
came to
this G
my nam
under th
fully do
the uppe
watchin
and we
sitting.
will pro
near hi

“I w
been d
I recal
all Ger
on sigh
bility t

I ask
of the
genera
thing
South
and pu
and cu

Dr
views
result
who
The
stigm
heavi
of ca
is to
of a
or N
fath

In
stan
gene
in F
him
time
ciate
Fre
stre
sex
one
eve
is p
I
wa
to
rep

politely and came back to where I was reading the newspaper. 'Is this you?' I asked, pointing to an article in the *London Times*. I put my right hand on his left sleeve and said: 'Curse you; curse you; curse you!'

'Then he walked away and two women, strangers, came to find out my name. They seemed to belong to this German. They did not believe me when I told my name and looked inside my dress where it was sewn under the left shoulder. They left, and I walked fearfully down the street. I entered an inn and went to the upper floor, looking down from there into the lobby, watching people come and go. Then I came downstairs and went into a room where a venerable bishop was sitting. 'I am afraid the invasion is on,' I said. 'God will protect us,' the bishop replied. A woman sitting near him kissed the ring on his hand.

'I woke up from the dream with the thought: 'I have been disobedient; I ought to have shot the German.' I recalled a statement in the English newspapers that all German soldiers appearing in England must be shot on sight. I thought at the time what a terrible responsibility that was."

I asked the patient for the most emotional element of the dream. She said it was the cursing of the Nazi general. She cursed him three times because everything happened to her in threes. When she was in South America, a man took her for a Nazi sympathizer and proposed a toast to Hitler. She lifted her glass and cursed: "To Hitler; may he rot in Hell!"

Dreams are not influenced by one's political views. Rather are one's political views the result of one's feeling attitude toward people who were in authority over one in childhood. The patient did not know her father, and the stigma of illegitimate birth was rendered heavier by her mother's noble blood and loss of caste on account of her love attachment. It is to be expected that to the unconscious mind of a patient so afflicted, Hitler or a Nazi general or Nazis in general should symbolize the devil father.

In the dream, the patient's concern with names stands out conspicuously. She asked the Nazi general if his name was Nègre, which is "Negro" in French. She obviously was intent on abusing him. By reading the *Times*, she hinted at past times as the source of her hostility. She associated with Negroes blackness and fear, and with French, sexual abnormality. Illegitimacy, by a stretch of imagination, could be considered a sexual abnormality. One can never quite divest one's mind from the notion that birth is a sexual event, and the patient observed that the *Times* is prominently used for birth notices.

I asked her to define cursing. She said it was the refuge of one who is absolutely helpless to do anything else. Cursing thus may well represent an infantile form of self defense.

She discovered in the same breath that the Channel may refer to the uterine passage and that the destruction of ships could represent the danger to her particular ship of life and could stand for the fear of death during the process of birth.

The father, however, is not involved in birth. The cursing is a superimposure, an element regressively associated with birth, an attempt at merging the physical shock with the moral one. She had an excellent motive for such regressive association. Her father did not give her his name; she had no right to it; she was on his "left" side. Left, in dreams, refers to that which is wrong, injurious.

The two women recalled the memory of two women tyrants in her life: her old nurse and the wife of her guardian. As tyrants they well belonged to the Nazi general. She could not remember her answer when the two women asked her name, but as they did not believe her one may assume that she gave her father's name, which she had adopted without legal right. She had this name sewn into her dresses, but not under her shoulder. Under the shoulder is the arm pit, a hairy hollow which has a hidden genital value, by transposition from below to above. In this particular case it was invested with a traumatic significance of its own. Some years before the patient had fallen victim to Yucatan fever, which resulted in semiparalysis of her left arm from the shoulder down. This furnished an excellent background for the psychic paralysis caused by her illegitimacy.

The inn and the upper floor appear to be picturesque allusions to the womb. While she was writing down the dream, the sentence tumbled into the patient's mind: "Jesus entered an inn and went to the upper floor." The association gives this part of the dream a transcendental touch; but as "transcendental" simply means another life, it may as well apply to the Great Before as to the Great Hereafter. The venerable bishop as a symbol of spiritual protection is a good representation of Providence, the good father in heaven, in opposition to the bad father on earth, who forgets to look after his child. No inn can better minister to the needs of its guests than the maternal body to the needs of the child. The invasion was on, and there was death in the Channel; but God's protection did not fail, or the dream would never have been dreamed. However, the Nazi general should have been shot on sight. As the asso-

ciations on awakening are considered part of the dream, the guise of wartime legality openly reveals the dreamer's death wishes against her father, who rendered her illegitimate.

The aggressive emotions revealed by the dream have been stored up in this patient's unconscious mind for half a century. She knew no way of releasing them and was not aware of their destructive character. They redounded on her as they redounded on the psychotic patient, but in a different and very odd form. She fell

into her mother's pattern and punished herself for hating her by becoming the mother of an illegitimate child herself.

It is said that the daughters of drunkards almost invariably marry drunkards, even though they had been exposed to a great deal of suffering on their father's account. It would be rather interesting to know what is the percentage of illegitimate motherhood among those who were born illegitimate.

The Park Central Hotel, Seventh Avenue (19).

In a
cussed
exper
histan
secon
ductio
patien
such a
traum
heada
locati
conclu
tamin
to th
major
In
result
nism
inject
such
ache
obser
the p
head

The
first v
outpat
The
partic
patien
such
latera
as yo
the r
subje
mg. o

Th
Labor
Fr
Hosp
Neur
and
I.
matic
Psych

EXPERIMENTAL EVIDENCE OF THE PHYSIOLOGIC MECHANISM OF CERTAIN TYPES OF HEADACHE

ARNOLD P. FRIEDMAN, M.D.

CHARLES BRENNER, M.D.

AND

H. HOUSTON MERRITT, M.D.

NEW YORK

In a previous communication,¹ two of us discussed the mechanism of headache produced experimentally by the intravenous injection of histamine, emphasizing the significance of the secondary rise in arterial pressure in the production of the headache. It was found that in patients suffering from post-traumatic headaches such an injection usually "reproduced" the post-traumatic headache (i. e., was followed by a headache which was the same in character and location as the usual post-traumatic one). The conclusion was drawn that the injection of histamine activated a physiologic mechanism similar to that concerned in the production of the majority of post-traumatic headaches.

In the present paper, we wish to report the results of further studies bearing on the mechanism of headaches produced by the intravenous injection of histamine and on the relation between such headaches and various other types of headache encountered clinically. From the facts observed certain conclusions can be drawn about the physiologic mechanism of several types of headache which are met with clinically.

MATERIAL AND METHOD

The experimental subjects fell into two groups. The first was comprised of patients who had come to the outpatient clinic with the chief complaint of headache. The second was comprised of subjects who had no particular complaint of headache and it included ward patients suffering from a variety of neurologic diseases such as multiple sclerosis, neurosyphilis, amyotrophic lateral sclerosis and peroneal muscular atrophy, as well as young, healthy hospital personnel. For each subject the resting arterial pressure was determined with the subject supine, and 0.1 mg. of histamine base (0.275 mg. of histamine diphosphate) was rapidly injected in-

travenously. The subject was asked to report anything he felt or tasted and was questioned about his symptoms from time to time. The systolic blood pressure was determined at frequent intervals in most cases for the first two minutes and once or twice thereafter.

In subjects in whom headache developed after the injection, the effects of various special procedures were studied.

The effect of pressure on the carotid artery was investigated by digital compression of one common carotid artery for about fifteen seconds. The test was not considered satisfactory unless pulsation was felt to be absent above the site of compression. After release the subject was questioned about the effect on the headache of both compression and release.

The effect of jugular compression was tested by winding a sphygmomanometer cuff about the neck and inflating it to 25 or 40 mm. of mercury (with 1 subject digital compression was used). The subject was then asked what the effect had been on the headache of both compression and release.

The effect of a second injection of histamine on the headache was tested by injecting a second 0.1 mg. of drug intravenously at the height of the headache.

In one group of subjects the scalp was anesthetized by subcutaneous injection of 25 to 30 cc. of a 2 per cent solution of procaine hydrochloride in a zone lying just above the eyes in front, above the ears laterally and over the occipital protuberance behind. As soon as the scalp thus encircled had become completely anesthetic, the usual intravenous injection of histamine was given and the result noted.

In another group of subjects, a painful lump in the scalp was produced by subcutaneous injection of 1 cc. of a 6 per cent solution of sodium chloride. An hour later, after the local pain had disappeared, the subjects received the usual intravenous injection of histamine.²

The effect of inhalation of a mixture of 10 per cent carbon dioxide and 90 per cent oxygen on the headache produced by injection of histamine was also investigated. The gas mixture was administered by the usual type of face mask for a period of two minutes, which was sufficient to produce extreme hyperpnea (of maximal depth and with a rate of 35 to 40 per minute). Each experiment began with a two minute period of inhalation. After the respiratory rate had returned to normal, histamine was injected. If headache developed, the patient again inhaled the carbon dioxide-oxygen mixture for two minutes, and the effect of this on the headache was noted. In a few instances the cerebrospinal fluid pressure was measured simultaneously with a lumbar manometer.

2. Dr. H. G. Wolff suggested this procedure.

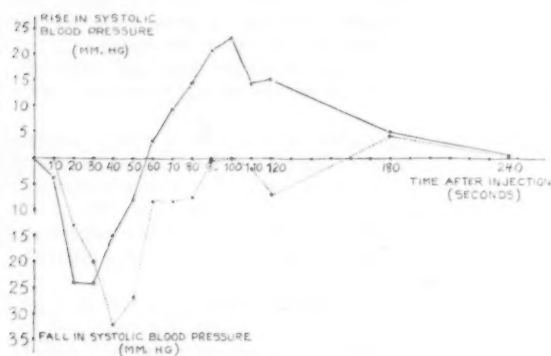
This study was aided by a grant from the Lederle Laboratories, Inc.

From the Division of Neuropsychiatry, Montefiore Hospital for Chronic Diseases, and the Department of Neurology, Columbia University College of Physicians and Surgeons.

1. Friedman, A. P., and Brenner, C.: Post-Traumatic and Histamine Headache, *Arch. Neurol. & Psychiat.* 52:126 (Aug.) 1944.

RESULTS

In 31 of 37 patients (38 of 46 injections) in whom the changes in the systolic blood pressure were closely followed, the intravenous injection of 0.1 mg. of histamine base was followed by a headache. In the other 6 patients no headache developed. In the figure the changes in arterial pressures in the two groups of patients are compared. It will be noted that the secondary rise in the group in which headaches developed was about equal to the initial fall (23 and 24 mm. of mercury, respectively), while there was no secondary rise in the group in which headache failed to develop.



Changes in systolic blood pressure following intravenous injection of 0.1 mg. histamine base (0.275 mg. histamine diphosphate). The solid line represents average values for 31 patients (38 injections) in whom headache developed after the injection; the dotted line represents values for 6 patients (8 injections) in whom such headache failed to develop.

Unilateral compression of the carotid artery was performed 18 times on 12 patients while they were experiencing experimentally induced headache. In 6 trials the headache disappeared completely during the period of compression, and in 9 trials it became milder. In 2 of the 9 trials the relief was experienced only, or in greater degree, on the side of the compression. In all 15 trials the pain returned when compression was stopped. In the remaining 3 trials compression failed to relieve the headache. In 1 of the patients, however, subsequent compression of the other carotid artery relieved the headache.

A second intravenous injection of 0.1 mg. of histamine base was given to 3 patients two to three minutes after the first. By that time the arterial pressure had returned nearly to normal and the headache was moderately severe. The second injection was followed by the usual prompt fall of arterial pressure, and the headache as promptly disappeared, to return as usual about a minute later, as the arterial pressure once more rose above the resting level.

Jugular compression was performed on 5 patients (7 trials) and failed to produce any change in the headache in any subject.

Nine patients inhaled a mixture of 10 per cent carbon dioxide and 90 per cent oxygen while experiencing headache. Six of these patients experienced no change in the headache during the inhalation. The other 3 patients experienced slight or moderate relief during the inhalation of the mixture. In 2 of these 9 patients and in 1 other who had no headache after the injection of histamine, the cerebrospinal fluid pressure was measured throughout the experiment by lumbar manometer with the patient lying flat on his side. It was found that inhalation of the carbon dioxide-oxygen mixture did not alter the arterial pressure but did raise the cerebrospinal fluid pressure from an average value of 65 mm. to an average value of 500 mm. of water (3 patients; 5 trials). The intravenous injection of 0.1 mg. of histamine in the same 3 patients raised the spinal fluid pressure from an average value of 67 mm. to one of 192 mm. The rise in spinal fluid pressure following injection of histamine was approximately synchronous with the fall in arterial pressure, as previously reported by Pickering.³

Complete anesthetization of the scalp by regional block failed to prevent the development of typical headache in 2 patients. One of these patients had had a previous injection of histamine without scalp block, and he reported that the second headache (after anesthetization of the scalp) was worse than the first had been.

Production of a painful lump in the scalp in 3 patients an hour or so before the intravenous injection of histamine did not apparently influence the location of the headache produced by the histamine. None of the 3 patients localized his headache to the region of the lump.

Twenty-two patients were questioned about similarity of the experimentally produced headache to previous headaches they had experienced as regards character and location of the pain. Twelve patients said the two forms were identical in these respects. In many of these patients the initial, painful pounding present during the secondary rise in arterial pressure following the injection bore no particular relation to the patient's usual headaches. However, as this pounding pain subsided, after one to several minutes, the residual pain (usually steady, though often still throbbing in character) was described by the patient as identical with his usual headaches. Two patients described the experimentally produced headaches as distinctly

3. Pickering, G. W.: Experimental Observations on Headache, *Brit. M. J.* 1:907 (May 6) 1939.

different from their usual ones, and one was undecided about the similarity. The other 7 patients had no clear memory of previous headaches.

The diagnostic classification into which these 15 patients' usual headaches fall is of interest. Both patients in whom the histamine did not reproduce the usual headache had no evidence of structural or vascular disease to explain their headaches, had many obviously psychoneurotic symptoms (anxiety, phobias, and/or compulsions, and/or hysterical conversion symptoms) and for many years had had recurrent headaches which bore no resemblance to migraine. This type of headache we classify as psychogenic. Five of the 13 patients in whom histamine reproduced the usual headaches fall into the same group. Closely allied to and perhaps indistinguishable from this group is another one of 5 patients who had occasional headaches of non-specific type (without accompanying structural or vascular disease), usually related to fatigue or emotional stress. One patient had headaches associated with Paget's disease (osteitis deformans) and increased intracranial pressure; 1 had occasional headaches which were always associated with the onset of an acute infection, and 1 had headaches once every two or three months, always on the first day of her menstrual period.

COMMENT

In most persons the intravenous injection of 0.1 mg. of histamine base (0.275 mg. of histamine diphosphate) is followed in sixty to ninety seconds by a headache which lasts a few minutes. In a previous article¹ two of us (A. P. F. and C. B.) discussed the sequence of physiologic changes following the injection which appear to be responsible for the appearance of headache. Briefly, the changes were these: Within a few seconds after the injection there are pronounced dilatation of the vessels of the upper half of the body, including the intracranial arteries, and a rapid fall in blood pressure (average, 24 mm. of mercury); a compensatory reflex then produces an increase in cardiac rate and a rise in arterial pressure above the resting level which is about equal to the original fall (figure); as the pressure rises above normal the headache begins, is most intense at about the height of the rise and lasts for a few to several minutes after return of the arterial pressure to normal. The headache is presumably due to stretching of the walls of the intracranial arteries, in which pain endings are known to lie, as the relaxed arteries are distended with blood driven in under increasing pressure.⁴

The role of the secondary (reflex) rise in arterial pressure in the production of headache following injection of histamine was emphasized in an earlier publication.¹ The observations here reported support the correctness of this view. In the first place, as shown in the figure, there was no secondary rise in the group of patients in which headache failed to develop. Next a second injection of histamine abolished the headache as long as the blood pressure was low. Finally, reduction of the cerebral circulation by temporarily occluding one carotid artery abolished or relieved the headache in the majority of subjects. The last two observations confirm those made previously by Pickering.³

Earlier authors³ have laid stress on the importance of changes in the cerebrospinal fluid pressure in the genesis of these experimentally produced headaches. It was felt that the fall in spinal fluid pressure to the resting level (which occurred at about the same time as the onset of the headache) deprived the extracerebral arteries of external support and allowed them to be distended more widely, and hence more painfully. In our experiments, however, the average fall in spinal fluid pressure following the injection of histamine was only 125 mm. of water or 9.2 mm. of mercury, which is much smaller than the average secondary rise in arterial pressure (23 mm. of mercury). Moreover, jugular compression failed to relieve the headache in any case, though the degree of compression used was such as ordinarily elevates spinal fluid pressure by 250 to 400 mm. of water (18 to 29 mm. of mercury). Finally, 6 of 9 patients failed to experience any relief of headache by inhaling the carbon dioxide-oxygen mixture, though the spinal fluid pressure was increased by this procedure by an average of 435+ mm. of water (32+ mm. of mercury) without change in intrarterial pressure. We conclude from these observations that alterations in the degree of support afforded the arterial walls by the external pressure of the cerebrospinal fluid is much less important in the development of headache following the intravenous injection of histamine than are the variations in arterial pressure which follow the injection.

Our previous observations¹ that in a number of patients with localized, unilateral, post-traumatic headache the injection of histamine "reproduced" the customary headache raised the question whether local injury to the scalp might somehow sensitize it to the action of histamine.

4. Schumacher, G. A., and Wolff, H. G.: Experimental Studies on Headache: Contrast of Histamine Headache with Headache of Migraine and that Associated with Hypertension, *Arch. Neurol. & Psychiat.* **45**:199 (Feb.) 1941. Pickering.³

We have found, however, that injury caused by injection of 1 cc. of a hypertonic solution of sodium chloride does not so sensitize the scalp, nor does anesthetization of the scalp by regional block with procaine hydrochloride affect or prevent the production of headache by injection of histamine. These observations substantiate the current view that headache following the intravenous injection of histamine arises from stimulation of pain fibers within rather than outside the skull.

We may now summarize our present understanding of the physiologic mechanism of this type of headache as follows: The pain arises from stimulation of pain endings (or fibers) which lie in or near the walls of the intracranial arteries. Previous authors⁴ have concurred in this conclusion. These structures are stimulated mechanically by the distention of the arteries, the degree of which is determined by two factors: the relaxation of the arterial walls and the rise in intra-arterial pressure. The first of these factors is caused directly by the action of histamine, whereas the second is produced by a secondary vasomotor reflex. The support (or lack of it) to the walls of the arteries by the pressure of the cerebrospinal fluid is of relatively slight importance.

The insight afforded by these observations and those of earlier workers into the physiologic mechanism of headache following intravenous injection of histamine is interesting from the point of view of pharmacodynamics alone, but it is also of considerable clinical significance. In a previous report¹ it was suggested that the physiologic mechanism in many cases of post-traumatic headache was probably similar to that of experimental histamine headache. The basis for this hypothesis was the observation that in many patients suffering from post-traumatic headaches the intravenous injection of histamine was followed by a headache which was identical in character and location with the customary ones of which the patient complained. The observations reported here indicate that the same holds true for many patients with psychogenic headaches, for patients with occasional headaches associated with fatigue and for the 1 patient each with menstrual headache, with headaches associated with Paget's disease of the skull and increased intracranial pressure and with headaches associated with the onset of an acute infection.

The hypothesis, therefore, seems justified that the physiologic mechanism in many cases of psychogenic headache associated with fatigue, as well as in many cases of post-traumatic headache, is similar to the mechanism of the headaches

produced experimentally by the intravenous injection of histamine, i.e., stimulation of the pain-sensitive structures lying in or near the walls of the intracranial arteries. To avoid any possibility of misunderstanding, it may be emphasized that this hypothesis does not imply that these clinical types of headache are caused by histamine or sensitivity to histamine. In the case of the experimentally produced headaches the pain-sensitive structures are stimulated mechanically as a result of circulatory and vascular changes. Perhaps the same may be true for some or all of the clinically recognized types of headache.

SUMMARY

A series of subjects comprised of patients with the chief complaint of headache, patients with a variety of organic neurologic diseases unrelated to headache and healthy controls received 0.1 mg. of histamine base (0.275 mg. of histamine diphosphate) by intravenous injection.

The headache which usually follows such an injection appears to be closely dependent on a secondary rise in blood pressure which follows the initial fall, as shown by (a) the absence of such a rise in patients in whom headache failed to develop, (b) the temporary disappearance or amelioration of the headache caused by compression of the carotid artery and (c) the temporary disappearance of the headache following a secondary injection of histamine.

Support (or lack of it) afforded the walls of intracranial arteries by the cerebrospinal fluid pressure seems to play a small part in the production of such headaches, as shown by the absence of improvement during jugular compression or, in most instances, during inhalation of an oxygen-carbon dioxide mixture.

The essential mechanism of experimentally produced histamine headache seems to be the mechanical stimulation of pain-sensitive structures in or near the walls of intracranial arteries, caused by distention of the relaxed walls by blood driven in under increasing pressure.

Twelve of 15 patients stated that the experimentally produced headache was identical with their usual headaches. In 9 of these 12 patients the usual headaches were related to emotional stress or fatigue; in 1, to Paget's disease of the skull with increased intracranial pressure; in 1, to onset of an acute infection, and in 1, to the menses.

Stimulation by whatever mechanism of pain-sensitive structures in or about the walls of the intracranial arteries would seem to be involved in the production of pain in many cases of chronic headache which are frequently met with in the clinic.

Montefiore Hospital for Chronic Diseases.

UNILATERAL INTERNAL OPTHALMOPLÉGIA: SOLE CLINICAL SIGN IN PATIENT WITH SYPHILITIC MENINGITIS

COMMANDER MEYER A. ZELIGS (MC), U.S.N.R.

AND

LIEUTENANT GERALD F. JOSEPH (MC), U.S.N.R.

The occurrence of any form of internal ophthalmoplegia always arouses the clinical interest and frequently presents itself as a diagnostic challenge to the examiner. It is well known that disturbances of ocular function, especially pupillary, are commonly encountered in patients with syphilitic involvement of the central nervous system. However, the presence of total internal ophthalmoplegia of one eye as the only clinical sign of syphilis of the central nervous system is extremely rare.

A review of the medical literature of the past decade (*Quarterly Cumulative Index Medicus*, 1935-1945) reveals no report in English describing such an occurrence. In 1935 Puglisi-Duranti,¹ a Spanish ophthalmologist, reported a total of 3 cases of internal ophthalmoplegia as an isolated clinical phenomenon. In 1937 he reported 1 additional case.² In 2 of these 4 cases the author described syphilis as the underlying cause of the ocular disturbance. The first case was that of an infant in whom the infection was congenital and the ophthalmoplegia was present at birth; the second case was one of acquired syphilis in which the ophthalmoplegia was bilateral. In the third case the ophthalmoplegia was unilateral and, according to the author, was "due to diabetes." In his subsequent report (1937) Puglisi-Duranti² described in detail the ophthalmologic, clinical and laboratory observations in a case of unilateral internal ophthalmoplegia. This disorder occurred in a "laborer" 33 years of age who presented himself for examination because of progressive diminution of vision of the right eye. The visual disorder was of six months' duration, and the patient had gradually lost his

ability to read with the right eye. Physical and neurologic examination revealed nothing else significant. Wassermann reactions of the blood and the spinal fluid were positive. Two months later ophthalmoscopic examination showed syphilitic chorioretinitis in both eyes. The unilateral ophthalmoplegia was still present and unchanged at that time.

Our purpose in presenting the following case is twofold: (a) to bring to the attention of clinicians, especially ophthalmologists and neurologists, the fact that total internal unilateral ophthalmoplegia may be the only presenting sign of syphilitic meningitis, and (b) to emphasize the importance of serologic examination of the blood and the spinal fluid whenever pupillary paralysis is encountered for which no obvious cause has been established, such as a history of encephalitis, ocular or intracranial trauma or the recent use of a mydriatic or cycloplegic drug. Such serologic tests should be made despite a negative history of exposure or complete absence of any previous syphilitic manifestations.

REPORT OF A CASE

D. D., a 25 year old Marine private first class, single, was admitted to the hospital for study on Jan. 6, 1945, because of an enlarged left pupil.

Present Illness.—For two weeks before admission to the hospital, the patient had noted blurring of vision in the left eye. About a week before admission he became aware that his left pupil was much larger than the right. No other symptoms or complaints were elicited.

Past History.—The patient had an attack of filariasis in December 1944, which was characterized by swelling, redness and aching of the right forearm, with enlargement of the right epitrochlear lymph node. This attack lasted about two weeks, and there had been no recurrence. There was no history of penile, oral or cutaneous lesions. A Kahn test made in February 1942 gave a negative reaction. There was no history of head injury or any acute illness suggestive of involvement of the central nervous system.

Mental Examination.—The patient was alert, intelligent, cooperative and affable. The psyche was normal, and he presented no complaints other than the mild disturbance of vision already described.

Physical Examination.—The patient was a well developed and well nourished white man. He did not appear ill. The skin and mucous membranes were

From Marine Barracks, Klamath Falls, Ore.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

1. Puglisi-Duranti, G.: Clinical Study on Internal Ophthalmoplegia, *Riv. oto-neuro-oftal.* **12**:256 (March-April) 1935.

2. Puglisi-Duranti, G.: Isolated Internal Ophthalmoplegia: Case Study, *Boll. d'ocul.* **16**:500 (May) 1937.

clear. The heart was normal, and the sounds were regular. The lungs were clear. The abdomen was soft, with no abnormal masses or tenderness. The genitalia were normal. The extremities presented no abnormality.

Neurologic Examination.—Both pupils were round and regular. The left pupil was widely dilated (6.5 mm.) and was completely fixed to light and in accommodation. Two drops of a 0.25 per cent solution of physostigmine salicylate produced prompt miosis. The right pupil was of normal size (3 mm.) and reacted well to light and in accommodation. The extraocular movements were full in all directions. There was no ptosis, nystagmus or strabismus. Fundusoscopic examination revealed an entirely normal condition.

The remainder of the cranial nerves were intact. The motor system was normal. The deep and superficial reflexes were present and of normal intensity; no abnormal reflexes were elicited. Sensation was entirely normal. Station and gait were normal. There was no stiffness of the neck.

Laboratory Data.—A Kahn test of the blood made on January 8, and repeated on January 11, gave a 3 plus reaction on both occasions.

Examination of the spinal fluid on January 9 revealed an initial pressure of 150 mm., a final pressure of 120 mm., normal dynamics, 60 cells (lymphocytes) per cubic millimeter, a Kahn reaction of 4 plus, a colloidal gold curve of 1112331000, a total protein of 49 mg. per hundred cubic centimeters and a sugar content of 80 mg. per hundred cubic centimeters.

Clinical Course.—The patient was transferred to another naval hospital. The results of studies of the blood and spinal fluid were strongly positive for syphilis. On this examination the spinal fluid contained 62 lymphocytes per cubic millimeter, and the colloidal gold curve was of the "high midzone type." The patient was given a course of 2,400,000 Oxford units of penicillin over a period of seven and one-half days. Three weeks after this treatment the clinical picture and the Kahn reaction of the blood were unchanged; the spinal fluid now showed only 10 lymphocytes per cubic millimeter, the colloidal gold curve was normal, and the Kahn reaction of the spinal fluid was less strongly positive than on the two previous occasions. Approximately seven weeks after completion of the treatment with penicillin, beginning reaction of the left pupil to light and in accommodation and decrease in its size were noted. A second course of 2,400,000 units of penicillin was given about two months after the first. Immediately after completion of this treatment the Kahn reaction of the blood was only slightly positive. The spinal fluid was not again examined.

On April 6, when the patient returned to duty, the pupil reacted nearly normally to light and in accommodation and was almost of the same size as the normal one.³

COMMENT

Syphilis obviously was the specific etiologic agent in this case. However, the pathogenesis of the ophthalmoplegia is not entirely clear, since the precise anatomic site of the lesion may be nuclear, basilar, radicular or of the peripheral neuron (including the ciliary ganglion and the postganglionic fibers). Since no anatomico-pathologic study was possible in this case, it is not within the scope of this report to enter into a discussion of the exact nature and localization of the pathologic process which produced the internal ophthalmoplegia. However, certain deductions which lie within the realm of clinical diagnosis are forthcoming. An ocular lesion (ciliary ganglion and iris) is ruled out by the demonstration of a normal pupillary response following the instillation of a miotic drug (2 drops of a 0.25 per cent solution of physostigmine salicylate was sufficient to produce miosis within about twenty minutes). Examination with the slit lamp revealed a normal iris. A basilar lesion (meningeal exudate) appears unlikely in view of the absence of other neurologic signs, particularly external ophthalmoplegia and ptosis. A nuclear or radicular lesion, therefore, seems the most probable, the pathologic process being either vascular or due to primary syphilitic involvement of one of the Edinger-Westphal nuclei.

SUMMARY

Isolated unilateral ophthalmoplegia may be the only clinical sign in a patient with syphilitic meningitis.

A case history illustrating such an occurrence is presented.

The diagnostic importance of serologic study in cases of unexplained pupillary paralysis is emphasized.

The rapid therapeutic response to penicillin therapy is mentioned.

The probable anatomic site of such a lesion is postulated.

3. Hasenbush, L. L., Lieut. (jg), U. S. Naval Hosp., Astoria, Ore.: Personal communication to the authors.

Sjös
trical a
of acet
strychn
and V
found
bromid
to the
duced
and M
demon
strong
out p
electri
pointe
those
lograp
of ele
seizur
patter
tion o
ner a
acetyl
causa
Ho
can b
(1)
seizu
(2)
phen
corte
are o
seizu
Fr
cal C
1.
Corte
and t
J. PH
2.
G. A
on th
1940.
3.
Effec
Pote
4.
Cert
Cort
1942

ACTION OF ACETYLCHOLINE ON MOTOR CORTEX

CORRELATION OF EFFECTS OF ACETYLCHOLINE AND EPILEPSY

FRANCIS M. FORSTER, M.D.

PHILADELPHIA

Sjöstrand¹ demonstrated an increase in electrical activity of the cortex on topical application of acetylcholine following previous application of strychnine and physostigmine. Miller, Stavraky and Woonton² and Chatfield and Dempsey³ found that 1 per cent solutions of acetylcholine bromide and chloride, respectively, applied locally to the previously physostigminized cortex produced an increase of electrical activity. Brenner and Merritt⁴ confirmed these observations and demonstrated that the cortical application of stronger solutions of acetylcholine chloride without previous physostigminization resulted in electrical discharges. Brenner and Merritt pointed out the similarity of these discharges to those encountered in clinical electroencephalographic studies, more particularly to the types of electrical activity found during grand mal seizures. Because of this similarity of electrical patterns and because the parenteral administration of acetylcholine can produce seizures, Brenner and Merritt suggested that disorders of acetylcholine metabolism may be important in the causation or mechanism of convulsive seizures.

However, before such an important deduction can be made, two further steps are necessary: (1) the correlation of experimental motor seizures with the acetylcholine discharges, and (2) the determination of other neurophysiologic phenomena known to be present in the epileptic cortex. In this investigation the experiments are concerned with the correlation of the motor seizures and acetylcholine discharges.

From the Department of Neurology, Jefferson Medical College.

1. Sjöstrand, T.: Potential Changes in the Cerebral Cortex of the Rabbit Arising from Cellular Activity and the Transmission of Impulses in the White Matter, *J. Physiol.* **90**:41P-45P, 1937.

2. Miller, F. R.; Stavraky, G. W., and Woonton, G. A.: Effects of Eserine, Acetylcholine and Atropine on the Electroencephalogram, *J. Neurophysiol.* **3**:131-138, 1940.

3. Chatfield, P. O., and Dempsey, E. W.: Some Effects of Prostigmine and Acetylcholine on Cortical Potentials, *Am. J. Physiol.* **135**:633-640, 1942.

4. Brenner, C., and Merritt, H. H.: Effect of Certain Choline Derivatives on Electrical Activity of the Cortex, *Arch. Neurol. & Psychiat.* **48**:382-395 (Sept.) 1942.

METHOD

In these experiments 28 cats were employed. All animals were anesthetized by the injection of Dial with Urethane⁵ in doses of 0.45 to 0.5 cc. per kilogram of body weight, one-half the dose being administered intraperitoneally and the other half intramuscularly. In studying the results of intracisternal injections of acetylcholine, one hemisphere was exposed over its anterior portion, so that bipolar silver-silver chloride electrodes could be placed over the cruciate gyrus (motor region), and records from the other hemisphere were obtained from steel phonograph needles driven into the intact skull. Acetylcholine chloride was injected intracisternally in amounts varying from 10 to 25 mg. after atropinization of the animals. For detailed studies of the motor cortex, the cruciate gyrus and adjacent areas of one hemisphere were exposed, care being taken to keep bleeding at a minimum. Stimulations were carried out by means of a Harvard inductorium, and bipolar platinum electrodes were used. The motor cortex was explored by stimulation until a region was found yielding a discrete response to stimulation, such as adduction of the shoulder, extension of the paw or flexion of the elbow. Bipolar recordings were obtained from two needles placed in the corresponding muscle. A unipolar silver-silver chloride electrode was placed on the same gyrus within 1.5 mm. of and equidistant from each of the stimulating electrodes. Acetylcholine chloride was applied in 5, 10 or 20 per cent solutions on filter paper pledgets, measuring 1 by 1.5 to 2 mm. These pledgets were carefully dried before application to remove any excess solution and were placed between the stimulating and the recording electrodes. As soon as acetylcholine discharges appeared, the pledgets were removed unless special observations on results of stimulation were to be made. In such instances the pledgets were left in place in order to avoid a complicating factor. All recordings were made by means of a three channel, condenser-coupled amplifier with an ink-writing oscillograph (Grass).

RESULTS

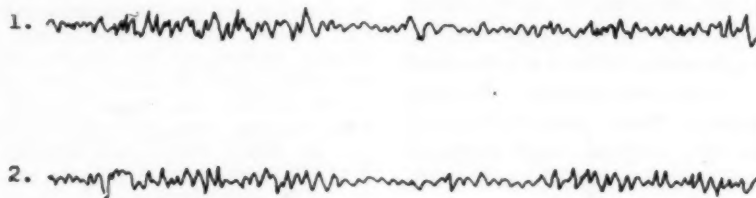
The intracisternal injection of acetylcholine into the atropinized cat resulted in a depression of electrical activity of the cortex, followed by a long-continued, high voltage, spiking discharge associated with generalized tonic-clonic convulsions. The electrical activity was of the type previously described as acetylcholine discharges. This type of activity was obtained not only from the needle electrodes in the skull but from bipolar silver-silver chloride electrodes over the previously determined motor cortex (fig. 1).

5. Dial With Urethane was supplied by Ciba Pharmaceutical Products, Inc.

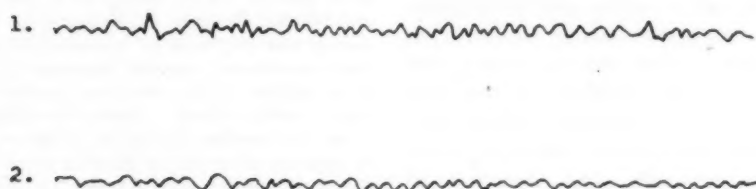
Direct application of acetylcholine to the motor cortex, as determined by stimulation studies, was less likely to produce discharges than application to the sensory cortex. Frequently, only a mild increase in electrical activity or scattered spiking occurred, despite the fact that in the same animal applications of acetylcholine to the sensory cortex produced typical discharges, with sharp onset and cessation. In the course of the experiments it was found that the response of the motor cortex to acetylcholine depended in large part on the depth of the anesthesia and the degree of loss

The motor component consisted of clonic movements simultaneous with the spiking activity of the cortex. These clonic movements were strictly limited to the muscle group thrown into contraction by electrical stimulation of the same area of cortex. Thus, if acetylcholine was applied to that region of area 4 which on stimulation produced flexion of the contralateral elbow, the clonic movements consisted of repeated flexion and relaxation of the elbow. The seizure did not spread to other portions of the extremity. In some instances in which anesthesia was very

Before ACh



50 sec. after ACh



180 sec. after ACh

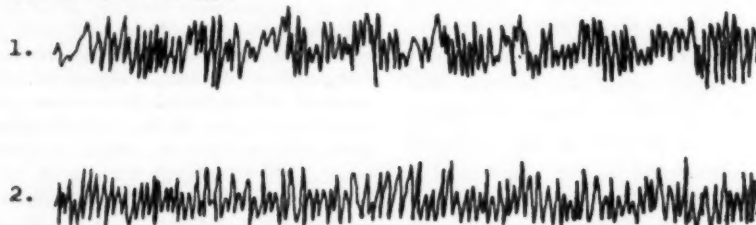


Fig. 1.—Electrocorticograms before and after cisternal injection of acetylcholine. 1 is a record from the right hemisphere through the intact skull; 2, a bipolar record from the previously explored left motor area.

Within fifty seconds after injection of acetylcholine there was a diminution of electrical activity, followed by rapid, high voltage, spiking discharges from both hemispheres. At the onset of this discharge there were generalized clonic movements of all extremities. The horizontal marker indicates one second; vertical markers indicate 500 microvolts.

of blood during preparation. When due regard was given to these factors and minute pledgets of filter paper moistened with acetylcholine were accurately placed, discharges could be obtained, and these were accompanied with motor evidence of seizures (fig. 2). The electrical discharges were identical with those previously described.⁶

6. (a) Forster, F. M., and McCarter, R. H.: Spread of ACh-Induced Electrical Discharges of the Cerebral

light the animal attempted to restrain the convulsing arm by placing the opposite paw on top of it.

Almost immediately after the application of acetylcholine, and before the appearance of the discharges, a depression of the electrical activity

Cortex, *Am. J. Physiol.* **144**:168-173, 1945; (b) The Effects of Local Application of Acetylcholine to the Acoustic Cortex, *J. Neuropath. & Exper. Neurol.*, to be published. (c) Brenner and Merriitt.⁴

of the cortex appeared. This was similar to the depression seen on intracisternal injection and to that previously described on application of acetylcholine to the parietal or the auditory receptive area of the cat cortex.^{6a,b} This depression of electrical activity was accompanied with decrease or absence of motor response to stimulation. The decrease in stimulability was transient, and its return did not depend on the removal of the pledget. When acetylcholine was placed at a distance, as on the middle suprasylvian gyrus, and a spreading depression of electrical activity was obtained, the motor response to stimulation of the motor cortex also decreased when the electrical activity of the motor area decreased. Strychninization of these distant areas did not in itself produce cortical suppression. During the period of acetylcholine discharges following application of the drug to the motor cortex, the motor response to electrical stimulation of the cortex was frequently

tate a light state of anesthesia, at least with the type of anesthetic used, and a ready stimulability of the motor cortex. The difficulties in producing motor and electrical discharge by the application of acetylcholine to the motor cortex may depend in large part on the anticonvulsant activities of the anesthetic employed. In any event, there is a sharp difference in the tendency of the motor cortex and that of the sensory cortex to respond with characteristic discharges to topical applications of the drug.

Since the motor discharges are temporarily correlated with the acetylcholine discharges, the application of the drug may be considered responsible for both. The seizures cannot be considered to arise on the basis of the systemic cardiovascular effects of acetylcholine, since atropinization does not prevent their appearance on intracisternal injection and since the motor response to topical application to the motor cortex is focal.

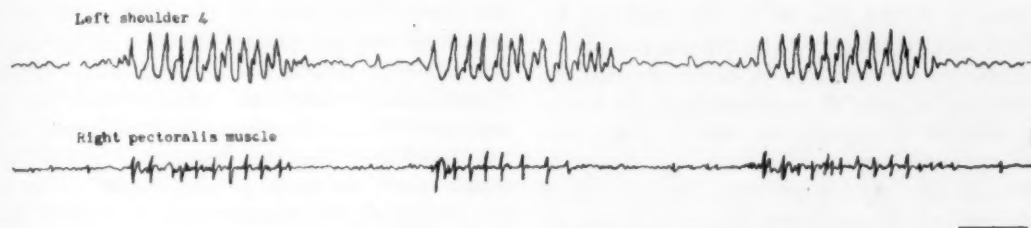


Fig. 2.—Electrocorticogram from the region of the left motor cortex stimulation of which yields discrete contraction of the right pectoralis muscle; electromyogram from the right pectoralis muscle. The record, taken during acetylcholine discharge, demonstrates cortical discharge with simultaneous discharge from muscle. Clonic movements of the right pectoralis muscle were apparent grossly during the recording. The horizontal marker indicates one second; vertical markers indicate 500 microvolts for the electrocorticogram and 200 microvolts for the electromyogram.

enhanced. Usually the responses remained localized to the same muscle group, but the range of movement was increased.

CONCLUSIONS

The convulsive seizures produced in the atropinized cat by the intracisternal injection of acetylcholine are accompanied with electrical discharges of the cerebral cortex of the type previously called acetylcholine discharges.^{6a} These discharges can be recorded not only through the intact skull but by bipolar recording from the exposed motor cortex, as previously determined by stimulation.

Under ideal conditions the application of acetylcholine to the motor cortex produces focal clonic convulsions accompanied with acetylcholine discharges. The convulsive movements are sharply limited in scope to the range of movement produced by electrical stimulation of the same region. The ideal conditions necessari-

The present contribution therefore links the motor seizure manifestations resulting from applications of acetylcholine with the electrical seizure manifestations. It is safe to say, therefore, that acetylcholine is truly a convulsant, that its activity as such is independent of its systemic action and is therefore a manifestation of its effect on the cerebral cortex and that the acetylcholine discharges are seizure discharges.

In the course of the past few years the role of acetylcholine in neuronal firing has been clarified to some extent. Fulton and Nachmansohn,⁷ in a recent review, pointed out the essential role of acetylcholine in the transmission of nerve impulses. Therefore, since acetylcholine is present in nerve tissue, is essential in transmission of nerve impulses and is a convulsant, the possibility is suggested that this substance, its forma-

7. Fulton, J. F., and Nachmansohn, D.: Acetylcholine and the Physiology of the Nervous System, Science 97:569-571, 1943.

tion and destruction, may play an important, if not the essential, role in the physiologic processes of epilepsy. If this is true, then the cortex treated with acetylcholine should reveal certain neurophysiologic phenomena of the cortex of the epileptic patient, as described by Penfield and his collaborators.⁸ These include neuronal transmission of seizure discharges, periods of increased and decreased stimulability and conditioning of the cortex. Forster and McCarter^{6a} demonstrated that the spread of acetylcholine discharges is along neuronal pathways, since the spontaneous or induced spread occurs in areas, as demonstrated by strychnine technic, in neuronal continuity with the primary area of application and since interruption of anatomic pathways prevents the spread. Studies of the acoustic cortex by Forster and McCarter^{6b} demonstrated sensory precipitation and sensory inhibition of the acetylcholine discharge and periods of decreased and increased auditory stimulability. Sensory precipitation for the somatic sensory cortex has been demonstrated by Chatfield and Dempsey.³ The role of conditioning of seizure transmission is obviously difficult to determine in acute experiments such as these. In the present studies on the motor cortex, decreased stimulability was found during the periods of depression of electrical activity. This decreased stimulability could not have been the result of a local phenomenon of the motor cortex, and therefore perhaps dependent on the presence of the pledget or of similar artefactual origin, since the stimulability returned to normal despite the continued presence of the pledget and since these alterations of stimulability occurred when the origin of depression was from a distant site, as on the middle suprasylvian gyrus. The application of strychnine to these distant areas without the development of depression of electrical activity or stimulability indicates that the depression did not arise from stimulation of one of the suppressor areas described by Dusser de Barenne and McCulloch,⁹ nor was it due to mechanical stimulation of the cortex as described by Leao.¹⁰ Further observations are being made on this

depression of electrical activity and cortical function. However, the close relationship between cortical depression and experimental seizure discharges has recently been stressed by Leao.¹⁰ Increased stimulability of the motor cortex has been demonstrated during the period of acetylcholine discharge.

Acetylcholine is therefore a convulsant. It holds the unique distinction among convulsant drugs of being normally present in the cortex. In addition, its presence is integrally related to neuronal firing. Its behavior as a convulsant is similar in its manifestations to that of the cortex of the epileptic patient. The logical deduction from these facts is that acetylcholine plays an important, if not the essential, role in the manifestations of epilepsy. Indeed, abnormalities of acetylcholine metabolism may well be the physiologic cause of epilepsy.

The major objection to this premise is the concentrations of acetylcholine employed in these, and in previous, studies. These concentrations are many times those of the cortex. Even the minimum concentrations effective in producing acetylcholine discharges after previous physostigminization¹¹ are much greater than the normal quantities. However, this objection need not invalidate the conclusions. Gerard¹² has shown that the isolated frog brain, when immersed for thirty minutes in a 1:100,000 solution of acetylcholine, presents unmistakable evidence of increased electrical activity. Obviously, it is not possible to handle in this manner cortex from which one expects to elicit motor or sensory responses. The discrepancy in effective concentrations may be due to difficulties in penetration of the solution through the intact pia-arachnoid and cortex to the neurons. Another factor is the cholinesterasic activity of the cortex, with rapid destruction of acetylcholine.

SUMMARY

The electrical discharges of the cortex produced by acetylcholine are similar to seizure discharges. These discharges can be correlated with the motor components of seizures. Variations of cortical stimulability, neuronal transmission of discharges, sensory precipitation and sensory inhibition have been correlated with acetylcholine discharges and epileptic discharges. Because of these observations and the normal presence of acetylcholine in the cortex, the view is taken that acetylcholine plays an essential role in the physiologic genesis of epilepsy.

Jefferson Medical College.

11. Sjöstrand.¹ Miller, Stavaky and Wootton.²

12. Gerard, R. W.: The Interaction of Neurones, Ohio State J. Sc. **41**:160-172, 1941.

8. (a) Penfield, W., and Erickson, T. C.: *Epilepsy and Cerebral Localization: A Study of the Mechanism, Treatment and Prevention of Epileptic Seizures*, Springfield, Ill., Charles C Thomas, Publisher, 1941, chap. 8, p. 625. (b) Penfield, W., and Boldrey, E. B.: Cortical Spread of Epileptic Discharge and the Conditioning Effect of Habitual Seizures, *Am. J. Psychiat.* **96**:255-281, 1939.

9. Dusser de Barenne, J. G., and McCulloch, W. S.: Factors for Facilitation and Extinction in the Central Nervous System, *J. Neurophysiol.* **12**:319-355, 1939.

10. Leao, A. A. P.: Spreading Depression of Activity in the Cerebral Cortex, *J. Neurophysiol.* **7**:359-390, 1944.

CHANGES IN CEREBRAL VEINS IN HYPERTENSIVE BRAIN DISEASE AND THEIR RELATION TO CEREBRAL HEMORRHAGE

CLINICAL PATHOLOGIC STUDY

I. MARK SCHEINKER, M.D.

CINCINNATI

There are few chapters in neuropathology of wider practical interest than that of hypertensive disease of the brain. This is mainly because arterial hypertension is a frequent associate of cerebrovascular accidents. The occurrence of massive hemorrhages in cases of arterial hypertension is familiar to clinicians and pathologists alike. With the exception of ruptured aneurysm, arterial hypertension is the condition most frequently associated with cerebral hemorrhage.

The histologic features of hypertensive disease of the brain have been described in detail.¹ In all cases typical alterations of the arterioles and capillaries were observed, which consisted of hyaline degeneration and fibrotic thickening of the wall and narrowing or complete obliteration of the lumen. It has been emphasized that these arteriolar alterations are different from those found with arteriosclerosis. The alteration of the nerve parenchyma consisted in diffusely scattered, small foci of old and recent softening, secondary to the arteriolar lesions.

While the arteriolar changes associated with hypertension have been relatively well studied, little or no attention has been devoted to the histologic changes in the veins.

This presentation is chiefly concerned with the venous alteration associated with hypertensive disease of the brain, which appears to have escaped much notice, though it is of frequent occurrence. The significance of the venous change in the origin of massive intracerebral hemorrhage is discussed.

MATERIALS AND METHODS

This presentation is based on a study of 65 typical cases of hypertensive disease of the brain associated with massive cerebral hemorrhage. In 52 cases there were large hemorrhagic cavities filled with blood; in 13 cases only small "ball hemorrhages" were found.

From the Laboratory of Neuropathology, Cincinnati General Hospital and the University of Cincinnati College of Medicine.

1. Scheinker, I. M.: Hypertensive Disease of the Brain, Arch. Path. 36:289 (Sept.) 1943; Zur Histopathogenese der Hirnapoplexie bei Hypertonie, Monatsschr. f. Psychiat. u. Neurol. 102:158, 1940.

The latter were also present in nearly every case of massive intracerebral hemorrhage in this series.

In the past most attention has been given to investigation of the extensive hemorrhagic areas, and attempts have been made to find the ruptured artery. It should be emphasized that in these areas all constituents of the brain parenchyma have been destroyed or secondarily changed by the invasion of large masses of blood. The vascular alterations in these areas cannot, therefore, indicate the preapoplectic state of the blood vessels.

In this study an attempt was made to examine the process in its earliest stages rather than later, when secondary destruction of tissue had occurred. For this

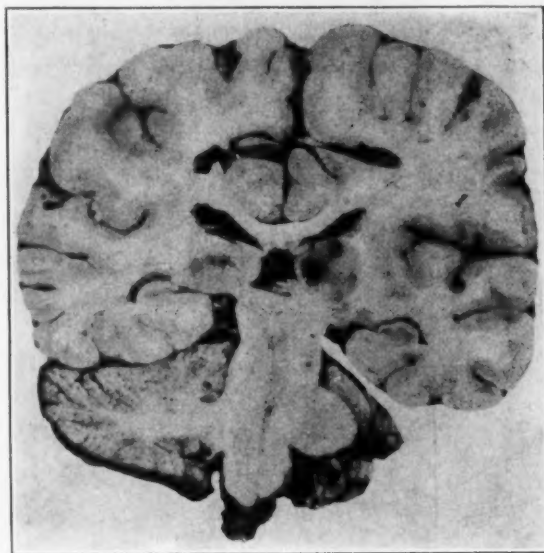


Fig. 1.—Two ball hemorrhages in the left pulvinar region and one in the cortical gray matter of the left parietal lobe.

purpose, large hemorrhagic lesions were excluded from investigation, and histologic analysis was limited to lesions which have been described as ball hemorrhages (*Kugelblutungen*). They represent a miniature form of massive hemorrhage, and because of their minuteness they offer a better opportunity for study of the primary vascular alterations.

Numerous sections taken from grossly intact areas of gray and white matter in the vicinity of the larger hemorrhages were also studied.

OBSERVATIONS

Ball Hemorrhages.—The gross changes, which were uniform in character, are well illustrated in

figure 1. Small, round or oval, sharply demarcated hemorrhagic foci could be seen scattered through the gray and white substance of the hemispheres. They varied from 10 to 50 mm. in diameter. In only a few instances could they be found in the vicinity of massive hemorrhages; their site was in areas far remote from the large hemorrhage cavities.

On microscopic examination, the ball hemorrhages, with but few exceptions, were found to consist of one or several blood vessels surrounded

sisting of white and red blood cells. The venous walls showed almost complete loss of stainability. In relatively few instances had the veins undergone complete disintegration, and then it was difficult to be sure of the source of the hemorrhage. No evidence of rupture of a vessel wall could be found in any of the ball hemorrhages.

The adjacent nerve parenchyma was with but few exceptions found to be fairly well preserved. It showed evidence of compression by the blood clot and an early stage of edema formation



Fig. 2.—A small central vein in a ball hemorrhage, showing almost complete degeneration and disruption of the vessel wall. Hematoxylin and eosin; $\times 55$.

by large masses of coagulated blood. These vessels were medium-sized, congested veins, the lumen of which was extremely distended, and far advanced degenerative changes had occurred in the wall. The degree of degeneration is illustrated in figures 2 and 3. The wall of the vein had undergone almost complete degeneration, and the blood within merged with the extravasated blood surrounding it. Some of the veins were surrounded by a zone of infiltration, con-

(figs. 2 and 3). Beyond this zone of compression there were no signs of preexistent softening or disintegration of tissue.

Healed Hemorrhages.—Microscopic studies disclosed numerous foci of glial proliferation in the vicinity of dense accumulations of blood pigment (fig. 4). The central region was composed of amorphous masses of blood pigment. The nerve parenchyma was completely destroyed; it contained no nerve cells or nerve

fibers
tion
packed
zone
work
of gli
paren
destr
follow
there

Not
toxy

A
Th
few
per
zon
act
of
vei
vas
int

fibers. The center was surrounded by a transition zone composed of numerous glitter cells packed with blood pigment. The peripheral zone of demarcation consisted of a dense felt-work of glial fibers with glial nuclei. This area of gliosis graded off gradually into normal nerve parenchyma. These represent focal areas of destruction of nerve tissue by a ball hemorrhage, followed by reactive glial change. They may, therefore, be designated as healed hemorrhages.

clasmotodendrosis and ameboid degeneration. The small perivenous hemorrhages are well illustrated in figure 5. The veins were maximally distended and engorged with blood, displaying signs of stasis; their walls showed extreme thinning and necrosis. In some of the veins there was to be seen a mere shadow of the wall; their content merged with the extravasated blood of the maximally distended perivascular spaces.

Only occasionally the massive hemorrhage was

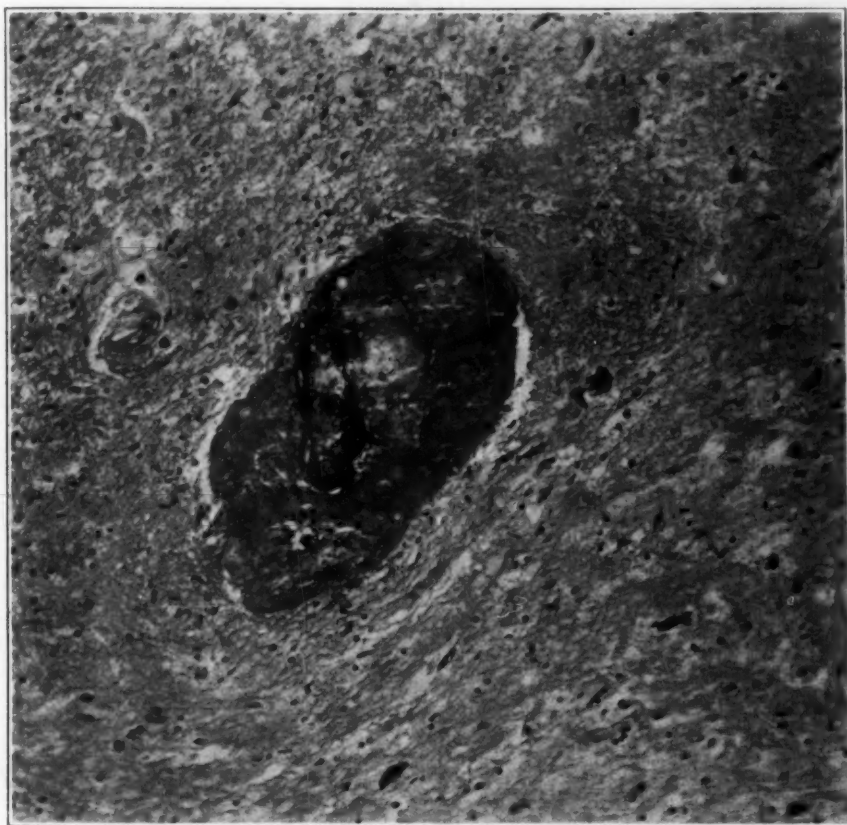


Fig. 3.—A ball hemorrhage, with the central vein represented by a mere outline of the disintegrated wall. Note the preservation of the adjacent nerve tissue, which showed only a moderate degree of compression. Hematoxylin and eosin; $\times 120$.

Extrahemorrhagic Changes in Nerve Tissue.—The large massive hemorrhage was, with but few exceptions, surrounded by numerous small perivenous hemorrhages (fig. 5) and by a large zone of advanced edema. The latter was characterized by an areolar, or sievelike, appearance of the tissue, maximal congestion of the smaller veins and capillaries, with distention of the perivascular spaces, and transudation of serous fluid into the nerve parenchyma; the glia displayed

found to be surrounded by a narrow zone of encephalomalacia, characterized by complete destruction of tissue and replacement with compound granule cells.

It seems appropriate at this point to indicate in passing some observations described in detail elsewhere. In about two thirds of the cases of massive intracerebral hemorrhage in this series there was associated edema of the brain stem and hemorrhage. The latter was predominantly peri-

venous in distribution and was associated with an extreme degree of venous congestion. Attention has been directed to a clinicopathologic condition described as "transtentorial herniation of the brain stem" responsible for the origin of the hemorrhages of the brain stem.²

Venous Alterations.—In all cases in which examination was made, the veins, particularly those of the central white matter and of the basal ganglia, showed three types of abnormalities, which were in some cases combined and in

and 7 show cerebral veins which display an extreme degree of distention of their lumens and signs of stasis. Their walls disclosed some evidence of degeneration. These relatively early vascular lesions appear to cast light on the pathogenesis of cerebral massive hemorrhage and should therefore be specifically emphasized. Figure 6 shows, in addition to the vascular alteration, the evidence of beginning reaction of the surrounding nerve parenchyma, characterized by rarefaction and an early stage of edema forma-

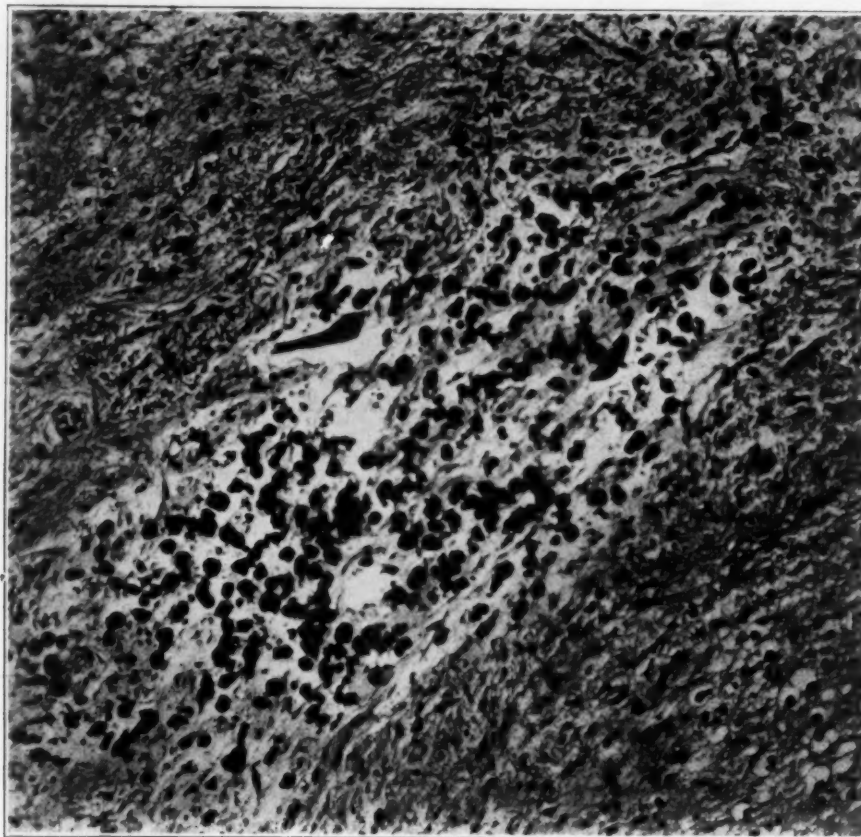


Fig. 4.—Healed hemorrhage, characterized by a focal area of glial scar formation about a dense accumulation of blood pigment. Hematoxylin and eosin; $\times 160$.

others observed separately: (a) congestion and stasis, associated with a tremendous distention of the lumen of the vein, (b) advanced atrophy, and (c) disintegration and necrosis of the wall of the vein.

Venous congestion and stasis were among the most frequently observed changes. Figures 6

and 7 illustrates more advanced changes, characterized by increased permeability of the maximally distended vein for red blood cells and serous fluid, associated with marked degeneration of the wall.

Advanced atrophic alteration of the cerebral veins was the rule (figs. 8 and 9). Figure 8 shows in cross section a large vein from the basal ganglia displaying an extreme degree of atrophy. The normal appearance of the division into three coats is completely lost. The entire vessel wall is

2. Scheinker, I. M.: Transtentorial Herniation of the Brain Stem: A Characteristic Clinicopathologic Syndrome; Pathogenesis of Hemorrhages of the Brain Stem, *Arch. Neurol. & Psychiat.* **53**:289 (April) 1945.

tremendously thinned out and is restricted to a thin connective tissue membrane. It is completely devoid of either muscular or elastic elements. It is bounded on the luminal margin by a few endothelial cells, which are barely visible. The differentiation between endothelial nuclei and those of the surrounding connective tissue membrane is obscured and cannot always be made. The perivascular space is distended and harbors a few nuclei of macrophages.

tureless, homogeneously stained, slightly translucent necrotic ring (fig. 10). It was by no means rare that certain parts of the vessel wall were reduced to an extremely thinned-out membrane, as though on the point of rupture. Cross sections of some of the larger veins revealed completely misshapen and disintegrated walls, bounded exteriorly by accumulations of blood pigment and degenerated, edematous and rarefied nerve tissue (fig. 11). The adventitia was frequently distended with extravasated blood, which

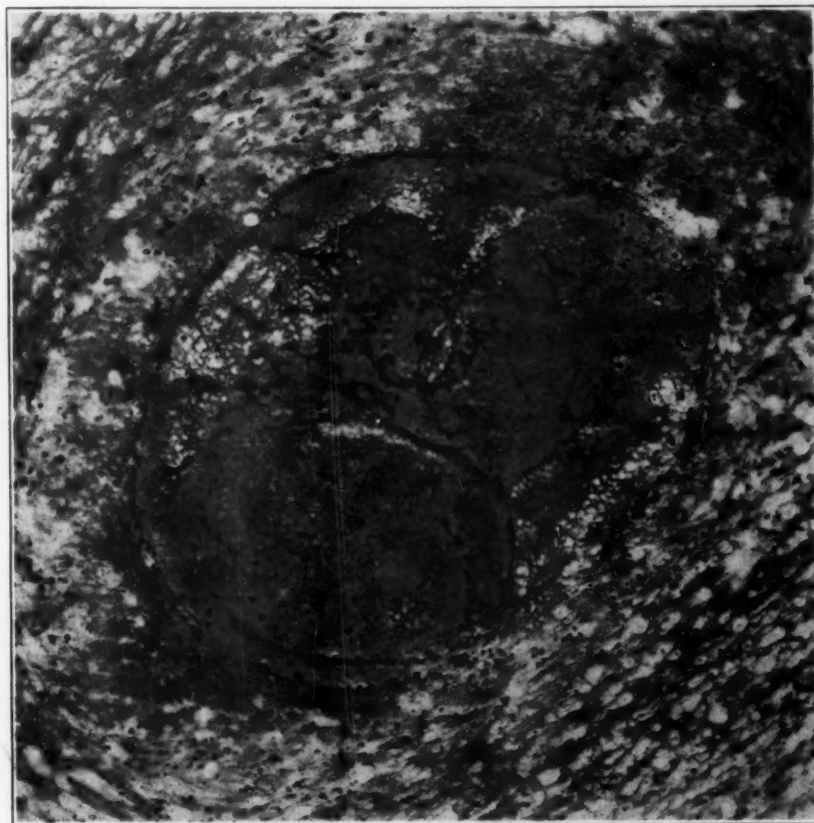


Fig. 5.—Perivenous hemorrhage and edema in the vicinity of a massive hemorrhage. Note the thinning and necrosis of the vessel wall. Hematoxylin and eosin; $\times 160$.

The atrophic changes of the smaller veins (fig. 9) were similar in nature. In contrast to the abnormal thickening of the smaller arterioles, the veins were conspicuously atrophied. Their wall consisted of a simple tube, containing a small quantity of connective tissue fibers and a hardly discernible layer of endothelial cells; there were no muscular or elastic elements.

The atrophic changes of the veins were frequently associated with necrobiotic alterations of the wall (figs. 10 and 11). In many veins the entire wall appeared transformed into a struc-

tureless, homogeneously stained, slightly translucent necrotic ring (fig. 10). It was by no means rare that certain parts of the vessel wall were reduced to an extremely thinned-out membrane, as though on the point of rupture. Cross sections of some of the larger veins revealed completely misshapen and disintegrated walls, bounded exteriorly by accumulations of blood pigment and degenerated, edematous and rarefied nerve tissue (fig. 11). The adventitia was frequently distended with extravasated blood, which

3. Charcot, J. M., and Bouchard, C.: Nouvelle recherches sur la pathogénie de l'hémorragie cérébrale, Arch. de physiol. norm. et path. 1:110, 643 and 725, 1868.

stant vascular change in brains with massive cerebral hemorrhage. Frequently the perivascular spaces were found to be tremendously distended and torn, permitting the escape of red blood cells and transudation of serous fluid into the surrounding tissue.

HISTORICAL REVIEW

Cerebral hemorrhage is one of the commonest and least understood pathologic conditions.

disease and expressed the opinion that an enzyme from the kidney might lead to autolysis of nerve tissue, thus creating an area of prehemorrhagic softening predisposed to cerebral hemorrhage.

Westphal and Bär⁵ were the first to call attention to the significance of functional vascular disturbances in the pathogenesis of cerebral hemorrhage. They advanced the idea that repeated angiospasm of one or more cerebral vessels was the probable cause of local ischemic

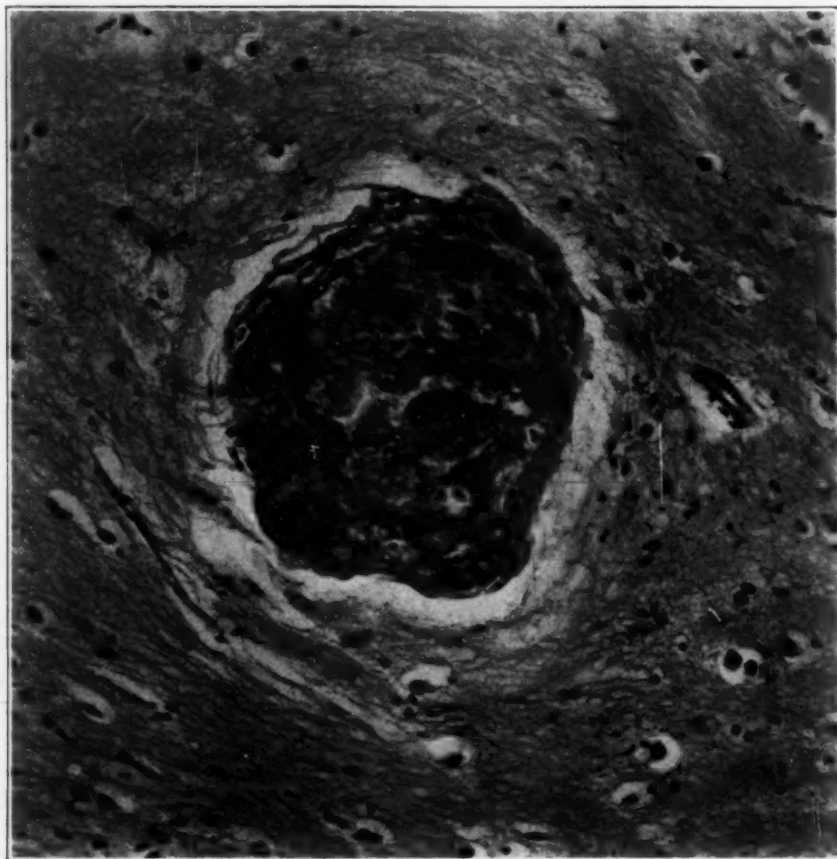


Fig. 6.—Extreme degree of venous congestion and stasis associated with partial disintegration of the wall. Note the rarefaction and edema of the surrounding tissue. Hematoxylin and eosin; $\times 160$.

Many theories have been offered to explain the pathophysiology. Charcot and Bouchard³ cited "miliary aneurysms," rupture of which they considered to be frequently associated with massive cerebral hemorrhage. Their concept was reflected in many textbooks, though this purely mechanical interpretation of the cerebral hemorrhage raised some objections.

Rosenblath⁴ pointed out the frequent coexistence of cerebral hemorrhage and advanced renal

changes in the nerve parenchyma. With the relief of spasm, the reopened blood vessel no longer had the support of a wall of firm brain parenchyma and hemorrhage might result.

4. Rosenblath: Ueber die Entstehung der Hirnblutung bei dem Schlaganfall, *Deutsche Ztschr. f. Nerven.* **61**:10, 1918.

5. Westphal, K., and Bär, R.: Ueber die Entstehung des Schlaganfalles, *Deutsches Arch. f. klin. Med.* **151**:1, 1926.

Schwartz,⁶ basing his opinion on the experimental observations of Ricker,⁷ expressed the belief that all embolic, arteriosclerotic and hypertensive hemorrhagic lesions are morphologic expressions of a common physiopathologic process. He stated the opinion that injury to nerve tissue is secondary to local circulatory disturbances, which may result from many irritants, and that these disturbances may be transmitted to remote areas of the brain by the nervous mechanism of the blood vessels.

hemorrhagic stage of softening must antedate the apparently abrupt and explosive vascular insult. They expressed the belief that the area of softening which existed before the hemorrhage for various lengths of time was probably caused by closure of a blood vessel in the course of a vascular disease of the brain.

SUMMARY OF THE PATHOLOGIC CHANGES

In the literature stress is laid on the arterial origin of cerebral hemorrhage. The present

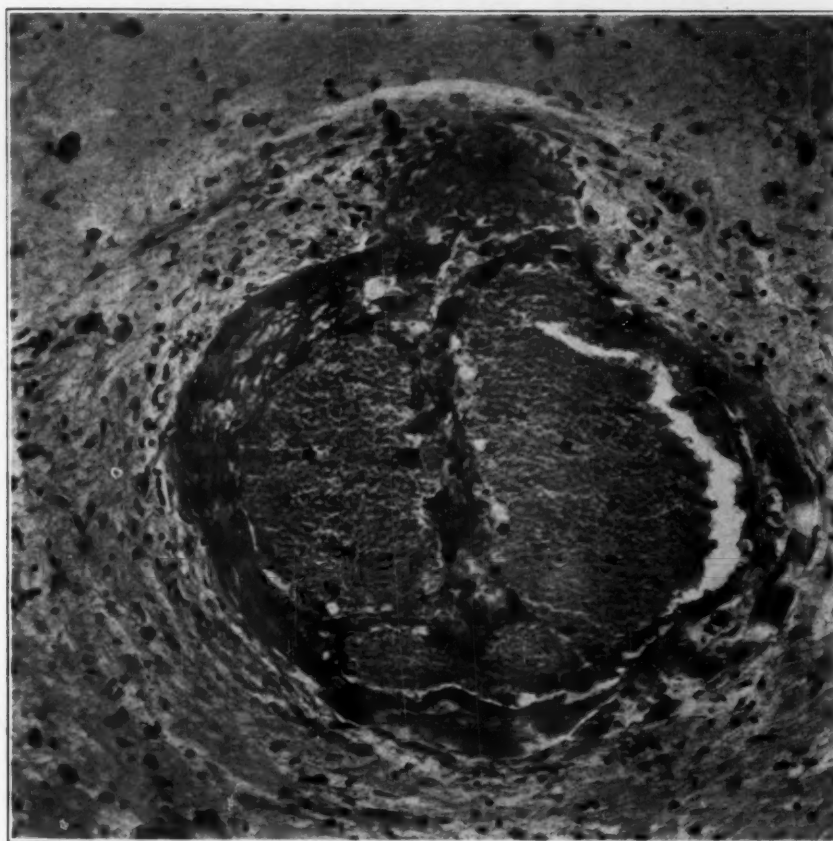


Fig. 7.—Increased permeability of a maximally distended vein for red blood cells and serous fluid. Note the degeneration and necrosis of the vessel wall. Hematoxylin and eosin; $\times 160$.

Globus and Strauss,⁸ after an extensive pathologic study, came to the conclusion that a pre-

6. Schwartz, P.: *Die Arten der Schlaganfälle des Gehirns und ihre Entstehung*, Berlin, Julius Springer, 1930.

7. Ricker, G.: *Die Entstehung der pathologisch-anatomischen Befunde nach Hirnerschütterung in Abhängigkeit vom Gefäßnervensystem des Hirnes*, Virchows Arch. f. path. Anat. **226**:180, 1919.

8. Globus, J. H., and Strauss, I.: *Massive Cerebral Hemorrhage*, Arch. Neurol. & Psychiat. **18**:215 (Aug.) 1927.

study has indicated that reversible, as well as permanent, structural alterations of veins may play a major role in the development of massive cerebral hemorrhage. From a microscopic study of a large number of ball hemorrhages the following points concerning their pathogenesis emerged:

Within a large majority of these hemorrhages there were one or several tremendously distended and congested veins, the walls of which displayed

advanced disintegration, with increased permeability for serous fluid and red blood cells. In only relatively few instances, and when the hemorrhagic lesion was more extensive, was it difficult or impossible to be sure of the source of the hemorrhage, mainly because of advanced disintegration of tissue and abundance of blood. In these lesions the veins were represented by a mere shadow of the wall, which had undergone almost complete degeneration, and the venous

of the type described by Charcot and Bouchard, were not found in the lesions examined.

The alterations of the veins were not confined to the areas of hemorrhage; in fact, these changes were found in areas far remote from the hemorrhagic lesions.

PATHOPHYSIOLOGY OF CEREBRAL HEMORRHAGE

A theory of the mechanism responsible for cerebral massive hemorrhage has been devel-

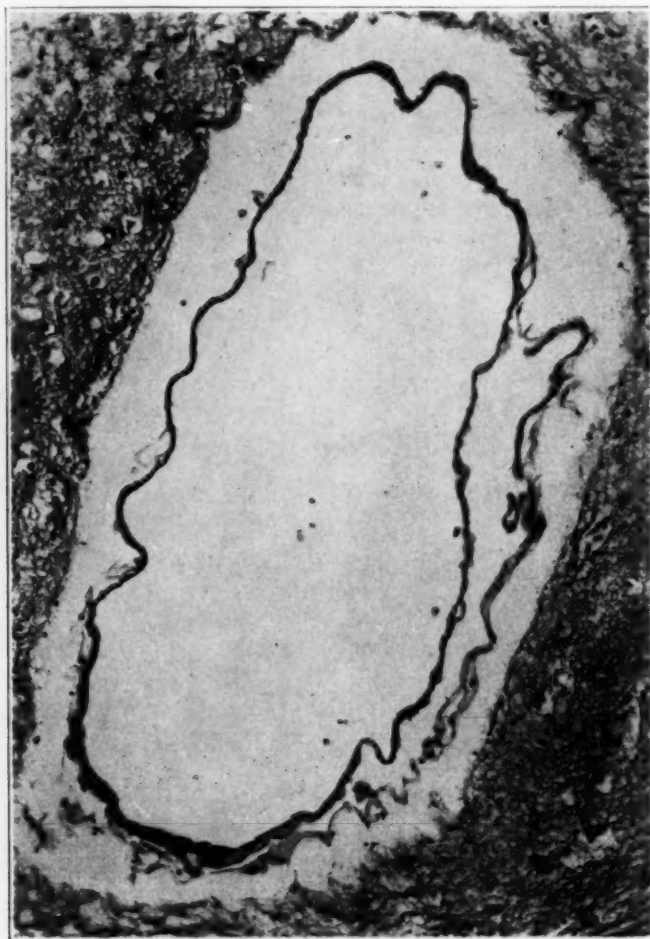


Fig. 8.—Cross section of a large vein from the basal ganglia displaying an extreme degree of atrophy. Hematoxylin and eosin; $\times 125$.

content was continuous with the extravasated blood.

In the extrahemorrhagic nerve tissue the changes consisted of compression and edema with but few exceptions. The majority of the hemorrhages were found to be outlined by a ring of edematous tissue. A zone of frank encephalomalacia could be detected in the vicinity of only some hemorrhagic lesions. Miliary aneurysms,

oped. In cases of arterial hypertension it is a terminal phase in a chain of events which has its beginning in reversible vascular disturbances of prolonged duration and repeated occurrence. These repeated vasoparalytic phenomena lead to stasis and congestion of veins and capillaries; it may be assumed that these vascular phenomena are at first transient and reversible. The effect of the repeated alterations in circulation, with

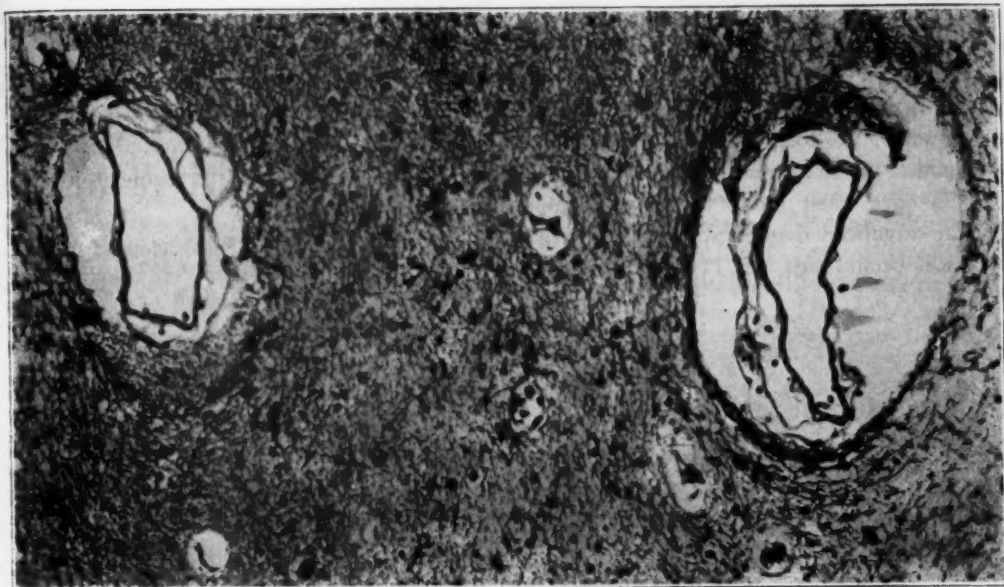


Fig. 9.—Atrophic changes of smaller veins. Hematoxylin and eosin; $\times 160$.

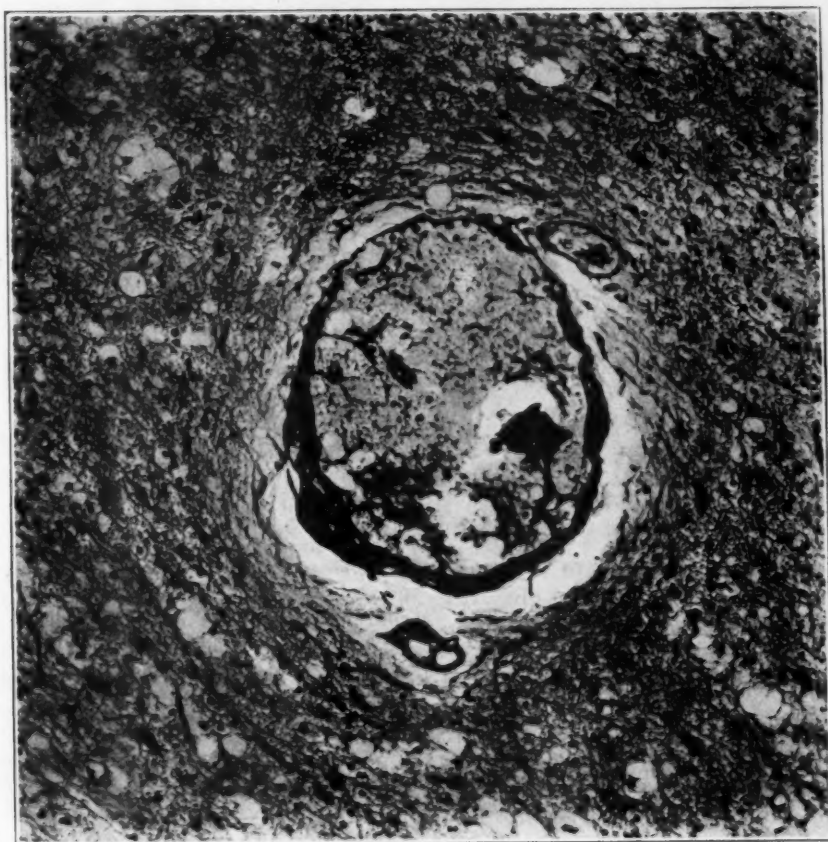


Fig. 10.—Far advanced degeneration of a maximally distended vein. The entire wall is transformed into a structureless, homogeneously stained, necrotic ring. Hematoxylin and eosin; $\times 160$.

prolonged periods of stasis and venous congestion, may finally result in structural lesions of the cerebral veins (distention and thinning and atrophy of the vascular wall). The changes, at first minimal, advance with each episode of slowing down of the local blood circulation and stasis, to which the inadequately nourished, thin-walled veins are most likely to be vulnerable. Finally, far advanced degeneration and necrosis of their walls occur (figs. 10, 11 and 12).

OCCURRENCE OF MASSIVE CEREBRAL HEMORRHAGE ASSOCIATED WITH OBSTRUCTION OF CEREBRAL VEINS

In view of the assertions made by some authors that massive bleeding must be arterial in origin, it seems appropriate to marshal additional evidence for the venous origin of cerebral hemorrhage.

A white woman aged 27 was admitted to the hospital because of repeated left-sided convulsions. Four weeks

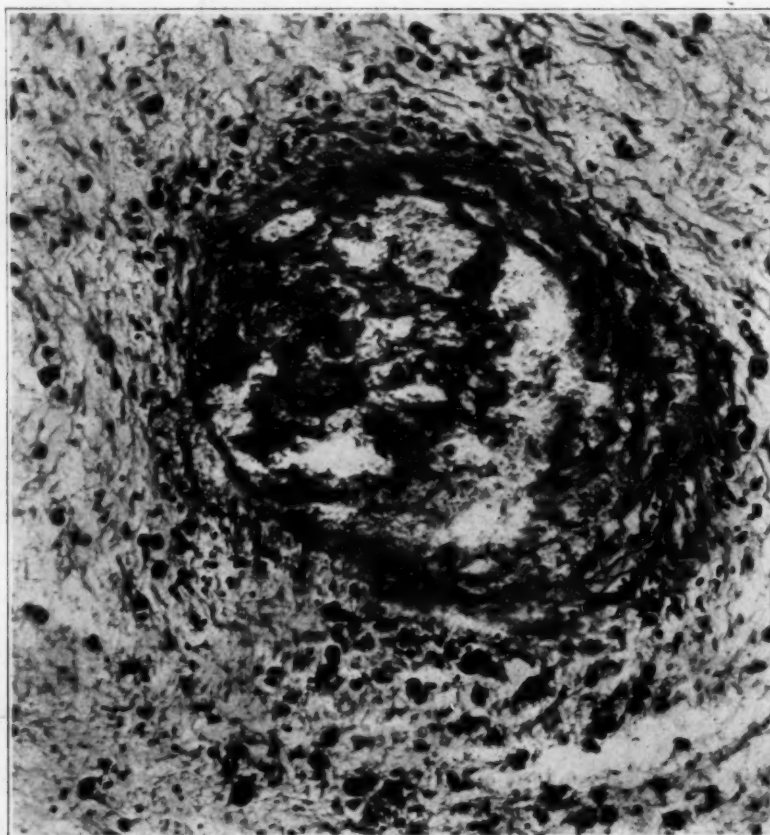


Fig. 11.—A larger vein with a completely misshapen and disintegrated wall, surrounded by a large accumulation of blood pigment and edematous nerve tissue. Hematoxylin and eosin; $\times 160$.

These veins are no longer able to withstand elevations of venous pressure and may give way at some points in their course, thus resulting in cerebral hemorrhage. The size of the resulting hemorrhage depends largely on the size of the altered vein. In areas in which only a small vein is involved the end result is the ball hemorrhage. If a large vein is involved, a gross hemorrhage results.

Data in support of this theory are furnished by the following observation.

before her admission edema had developed, which progressed from the right wrist and finally involved the entire right upper extremity, the breast and the right side of the face. During her stay in the hospital flaccid paralysis of the left extremities developed. The patient died on the seventh day in the hospital, with signs of pulmonary edema.

Gross examination of the brain revealed striking fullness of the veins over the right cerebral hemisphere, some of which measured 2.5 cm. in width. There were marked dilatation and tortuosity of the smaller veins. The right hemisphere was considerably larger than the left. Coronal sections of the brain revealed an extensive

massive he
of the right

Microsc
of the la
degree of
the right
closed typ
were cha
perivenou

The
lesions i
vincingl

Fi
surro

GEN

K
for
izati
The
been

rha
Fiv

massive hemorrhage, involving chiefly the white matter of the right frontal, parietal and occipital lobes (fig. 13).

Microscopic examination disclosed thrombosis of some of the larger pial veins (fig. 14) and a tremendous degree of passive congestion and stasis of all veins of the right hemisphere. Whereas the cortical ribbon disclosed typical softening, the lesions in the white matter were characterized by a large number of coalescent perivenous hemorrhages.

The occurrence of extensive hemorrhagic lesions in association with venous stasis was convincingly demonstrated by Cobb and Hubbard.⁹

cerebral injury¹¹ and infectious processes¹² ("meningoleucoencephalitis"). The effects of thrombosis of the smaller veins have been recently described under the heading of "vaso-thrombosis."¹³

The selective involvement of the white matter in cases of fat embolism,¹⁴ arsphenamine encephalopathy,¹⁵ carbon monoxide intoxication,¹⁶ late post-traumatic changes¹⁷ ("atrophic sclerosis of the white matter"), cerebral swelling and edema¹⁸ and diffuse sclerosis of the white mat-

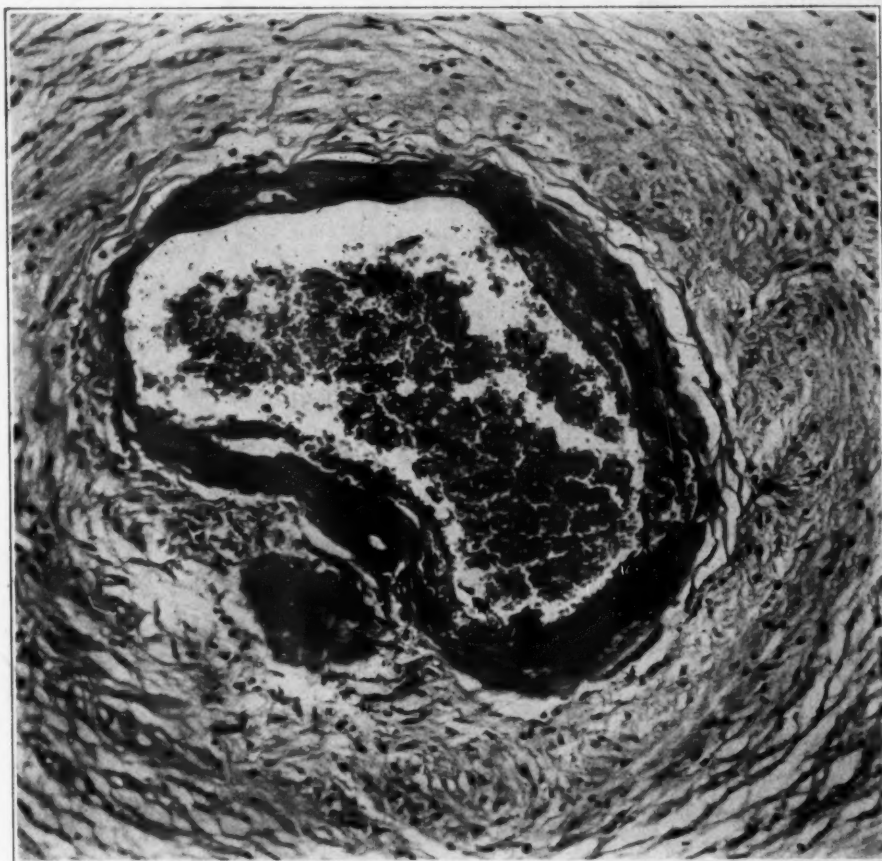


Fig. 12.—Adventitia of a vein distended with extravasated blood, merging with a small hemorrhage of the surrounding nerve parenchyma. Hematoxylin and eosin; $\times 160$.

GENERAL PRINCIPLES OF VENOUS DRAINAGE OF THE BRAIN

Knowledge of the venous system is required for an understanding of the predominant localization and distribution of cerebral hemorrhage. The importance of the venous circulation has been emphasized in cases of multiple sclerosis,¹⁰

9. Cobb, S., and Hubbard, J. P.: Cerebral Hemorrhage from Venous and Capillary Stasis: Report of Five Cases with Autopsy, *Am. J. M. Sc.* **178**:693, 1929.

10. Putnam, T. J.: The Pathogenesis of Multiple Sclerosis: A Possible Vascular Factor, *New England J. Med.* **209**:786, 1933; Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, *Arch. Neurol. & Psychiat.* **33**: 929 (May) 1935; Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," *ibid.* **37**: 1298 (June) 1937. Scheinker, I. M.: Histogenesis of the Early Lesions of Multiple Sclerosis: I. Significance of Vascular Changes, *ibid.* **49**:178 (Feb.) 1943.

(Footnotes continued on next page)

ter¹⁰ has been largely explained by the character of the vascularity of the white matter.

Whereas the cortical gray matter is supplied by a tremendously dense network of capillaries, the blood supply of the white matter is composed chiefly of vascular channels of considerable length, the anastomoses of which are scanty as compared with those of the cortex. The great majority of the large vessels of the white matter are veins. In serial sections, Alexander and Putnam¹⁰ were able to demonstrate that the large veins of the white matter drain into the venae striae terminalis and thence into the vena magna of Galen.

It is obvious that the effects of retarded circulation occurring with "vasoparalysis" or "vasothrombosis" are more apt to be observed in the poorly vascularized white matter than in the gray substance, which is richly supplied by an arborized vascular network.

Duret²⁰ described the long veins of the white matter as *veines medullaires*, but he did not note their topographic arrangement. Pfeifer,²¹ who

described these veins as *Markvenen*, made the general statement that a certain amount of the venous blood of the white matter was not drained by the surface veins but flowed toward the ventricles.

Schlesinger,²² in his interesting experimental study on venous drainage of the brain, referred to the large venous channels of the white matter as "intracerebral anastomotic veins." They

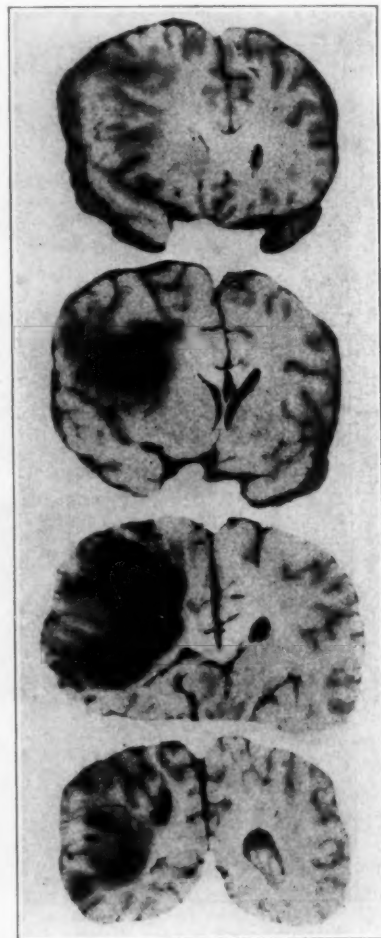


Fig. 13.—Extensive massive hemorrhage involving chiefly the white matter of the right hemisphere.

arise in the region of the angle of the lateral ventricle and establish the main intracerebral connections between the great vein of Galen and the veins of the surface of the brain. The cali-

11. Scheinker, I. M.: Vasoparalysis of the Central Nervous System: A Characteristic Vascular Syndrome, *Arch. Neurol. & Psychiat.* **52**:43 (July) 1944.

12. Scheinker, I. M.: Leucoencephalitis Associated with Purulent Leptomenigitis (Meningoleucoencephalitis), *J. Neuropath. & Exper. Neurol.* **4**:164 (April) 1945.

13. Scheinker, I. M.: Vasothrombosis of the Central Nervous System: A Characteristic Vascular Syndrome Caused by a Prolonged State of Vasoparalysis, *Arch. Neurol. & Psychiat.* **53**:171 (March) 1945.

14. Scheinker, I. M.: Formation of Demyelinated Plaques Associated with Cerebral Fat Embolism in Man, *Arch. Neurol. & Psychiat.* **49**:754 (May) 1943.

15. Scheinker, I. M.: Genesis of Encephalopathy Due to Arsphenamine, *Arch. Path.* **37**:91 (Feb.) 1944.

16. Scheinker, I. M.: Lesions of the White Matter of the Central Nervous System, to be published.

17. Evans, J. P., and Scheinker, I. M.: Histologic Studies of the Brain Following Head Trauma: IV. Late Changes; Atrophic Sclerosis of the White Matter, *J. Neurosurg.* **1**:306, 1944.

18. Scheinker, I. M.: Cerebral Swelling and Edema Associated with Cerebral Tumor, *Arch. Neurol. & Psychiat.* **45**:117 (Jan.) 1941.

19. Alexander, L., and Putnam, T. J.: Pathological Alterations of Cerebral Vascular Patterns, *A. Research Nerv. & Ment. Dis., Proc.* **18**:471, 1938.

20. Duret, H. M.: Recherches anatomiques sur la circulation de l'encéphale, *Arch. de physiol. norm. et path.* **6**:60, 316 and 664, 1874.

21. Pfeifer, R.: *Die Angioarchitectonik der Grosshirnrinde*, Berlin, Julius Springer, 1928.

22. Schlesinger, B.: The Venous Drainage of the Brain with Special Reference to the Galenic System, *Brain* **62**:274, 1939.

ber of these large veins does not appreciably change during their course. According to Schlesinger, the large anastomotic veins do not break up into capillaries but are joined only at relatively long intervals, and in most instances at right angles, by short venules. A second group of large veins can be seen in the basal ganglia, which he called longitudinal lenticular veins. Some of them perforate the internal capsule and reach the lateral surface of the put-

amen, traversing the outer layers in this structure. Their distribution is shown in figure 15. The large lenticular veins leave the substance of the putamen, enter the external capsule and open into the deep sylvian veins. Schlesinger noted that injected veins in the basal ganglia in man grossly resemble those in the monkey. That areas involved by hemorrhages, although varying in exact location in individual cases, are most frequently encountered in the general neighborhood affecting the thalamostriatal region. Next in frequency are the hemorrhages in the cerebral white matter and in the brain stem. The latter are most frequently secondary to transtentorial herniation of the brain stem.² The hemorrhages of the cerebral white matter are associated with occlusion of larger superficial veins.

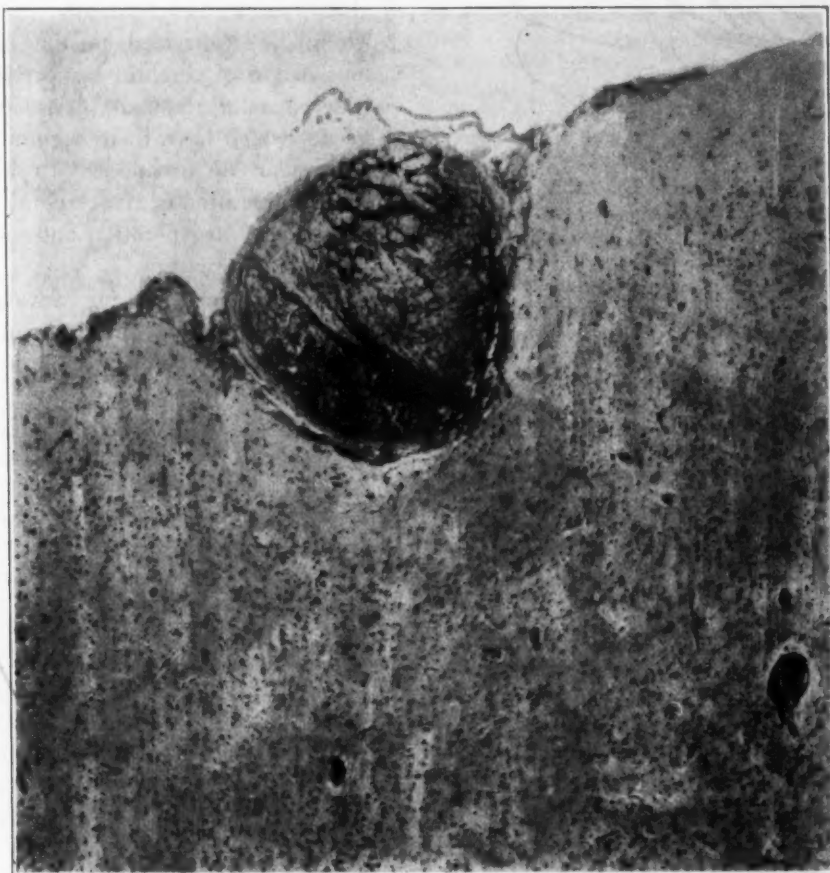


Fig. 14.—Thrombosis of a pial vein. Cresyl violet; $\times 85$.

amen, traversing the outer layers in this structure. Their distribution is shown in figure 15. The large lenticular veins leave the substance of the putamen, enter the external capsule and open into the deep sylvian veins. Schlesinger noted that injected veins in the basal ganglia in man grossly resemble those in the monkey.

PREDOMINANT LOCALIZATION OF MASSIVE HEMORRHAGES

In theory any cerebral blood vessel may be the source of hemorrhage. It is generally known

Many theories have been offered to explain the frequent occurrence of hemorrhages in the thalamostriatal region. The following explanation emerges from the present study: The size of the hemorrhagic lesion depends largely on the size of the altered blood vessel. It has been demonstrated that the largest veins are found within the basal ganglia (longitudinal lenticular veins) and in the central white matter (intracerebral anastomotic veins). This localization of the large veins may explain at least in part the predominant occurrence of massive

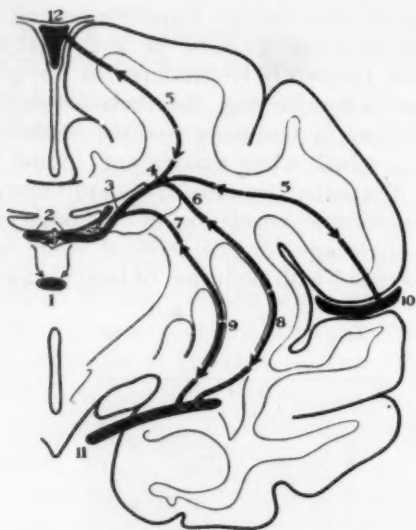


Fig. 15.—Diagrammatic distribution of large lenticular veins perforating the internal capsule and the basal ganglia in the brain of the rhesus monkey. 1 is the great vein of Galen; 2, small veins of Galen; 3, transverse caudate vein; 4, longitudinal caudate vein; 5, venous channels, connecting the great vein of Galen with the superior longitudinal sinus and the superficial sylvian vein; 6 and 7, superior external and internal lenticular veins; 8 and 9, inferior external and internal lenticular veins; 10, superficial sylvian vein; 11, deep sylvian vein, and 12, superior sagittal sinus. From Schlesinger.²²

hemorrhages within the basal ganglia and the white matter.

SUMMARY

The venous alterations associated with hypertensive disease of the brain have been studied in 65 cases, in most of which there were two types of lesions: (a) reversible changes, manifested by venous congestion and stasis, resulting in tremendous distention, and (b) structural alterations of the vessel wall, characterized by an extreme degree of atrophy and advanced signs of degeneration and necrosis.

Attention is directed to the predominantly venous origin of cerebral hemorrhage, which is considered as a terminal phase in a sequence of events which have their beginning in reversible vascular disturbances. In a later stage structural alteration of the cerebral veins occurs, and terminally degeneration and necrosis of the vessel wall are present.

In the presence of far advanced venular atrophy elevation of venous pressure would appear to be an essential precursor to the massive escape of blood.

Cincinnati General Hospital.

Since
therapy
shock b
frequen
mate o
seizures

The
logic ch
stantial
the pro
in the
induced
have c
cerebra
of sho
from e
demnat
posed
seizure
posed.
that c
are ele
ing th
eviden
on the
drama
usuall

In
follow
of the
imme
treatm
intelle
best m

Th
find m
receiv
any c

A
Patto
Marc

F

PSYCHOLOGIC STUDIES ON A PATIENT WHO RECEIVED TWO HUNDRED AND FORTY-EIGHT SHOCK TREATMENTS

JOSEPH PERLSON, M.D.

Chief of Neuropsychiatry San Bernardino County Hospital

SAN BERNARDINO, CALIF.

Since Sakel's discovery of insulin shock therapy, in 1933, and the introduction of electric shock by Cerletti and Bini, in 1938, the most frequent questions asked are: What is the ultimate effect of repeated induced convulsive seizures? Are organic changes produced?

The investigators who have reported histologic changes in the brain have not been in substantial agreement with each other. Whereas the problem of damage to the brain looms large in the minds of some investigators who have induced convulsive seizures in animals, others have carried out similar experiments with no cerebral injury. The opponents and proponents of shock therapy have sparred back and forth from enthusiasm to conservatism, and even condemnation. There are those even who have posed the possibility that electrically induced seizures lead to epilepsy in a person so predisposed. Nevertheless, there is sufficient evidence that cerebral function is disturbed. Not only are electroencephalographic changes present during the treatment, but the mental changes give evidence of organic changes. Still, most effects on the whole are reversible, and even the most dramatic mental symptoms of organic origin usually disappear eventually.

In view of this disagreement, it is necessary to follow the patients who have received this form of therapy and to observe the results not only immediately, but months and years, after the treatment. It must be ascertained whether their intellectual performance is on a level with their best normal activity.

The following case is presented because I can find no report in the literature in which a patient received so many induced convulsions without any discernible intellectual or physical sequelae.

REPORT OF A CASE

A white man, aged 27, was first admitted to the Patton State Hospital as a voluntary patient on March 15, 1942. The anamnesis obtained from a

From the Patton State Hospital, Patton, Calif.

brother was essentially as follows: The first symptoms of mental illness became known in April 1937, on receipt of a cablegram from the American Consul in Shanghai. Prior to this, the patient had left in August 1936 to attend school in Germany, but, because of the gathering war clouds, he left a short while later for China. He called on the Consul for help because he felt he was being followed and voices were calling him from the street lamps. Soon after, he jumped from the second story of a boarding house in an attempt to run away from imaginary followers and received fractures of the right arm, the patella and the ankle. Previously he had locked himself in his room and would not eat.

His relatives made the trip to China and brought him back. Because he was disturbed, he required mechanical restraint much of the way. On his return he was taken to a sanatorium but was removed in October 1937. After this, he became suspicious of strangers and took jaunts into the hills with his dog, staying away from two to five days at a time, regardless of weather conditions. He joined the Y. M. C. A. to make himself physically fit and got a job in an airplane factory, from which he was soon discharged.

He then left home and worked on a grape ranch. When the season was over, he returned and went to the California Institute of Technology to do postgraduate work. There he received credit for completion of one-half the work required for the degree of Master of Arts. In February 1941 he enlisted to become a flyer at an aviation school and graduated in September 1941. He was then stationed at McClellan Field, in Sacramento, as an Army transport pilot. From there he went east on maneuvers but was grounded in December because of an argument with an officer. Several weeks later he was sent to the Letterman General Hospital.

When seen in January 1942, he was delusional and suspicious of both officers and physicians. In February he was removed from the hospital and brought to southern California. After this, he would not converse and would not drink water or eat solid food, although he drank large quantities of milk and ate some bread. He claimed he was cold and kept the house at 75 F. while sitting on the floor radiator. He would not engage in any activities, because he asserted he was wired and it would disturb other people. He wanted his ear drums punctured so that he would be deaf and thereby his troubles would disappear. He had placed salve in his ears and stuffed them with paper. He believed that he was changing from man

to woman, that his breasts were enlarging and that he was losing his beard.

On the day of admission to the Patton State Hospital, he was resistive and assaultive and stated that he could not stand confinement. The next day he demanded his release, fought and kicked and attempted to break out of the door. He then became catatonic, refusing to talk or eat and required tube feeding. Two days later he was discharged and legally committed.

Because of his disturbed condition, a mental examination was not made. The working diagnosis was dementia praecox, paranoid type with catatonic features. The general physical and neurologic examinations revealed an essentially normal status. The blood pressure was 128 systolic and 80 diastolic. The results of routine laboratory examinations, including the Wassermann test of the blood and urinalysis, were also normal.

The patient was in and out of restraint for a total of one hundred and fifty-three days, from March 16, 1942 to May 22, 1944. The following reasons were given: He was combative, assaultive, destructive and delusional. He imagined that people were talking about him, framing him and calling him a sexual pervert and other names; that his brothers were in the ward and demanding that they be brought to him; that people were putting a radio beam on him and trying to destroy his mind; that government officials were waiting for him in the office; that the hospital was being bombed by planes. He was dangerous to himself in that he butted his head against the walls and pounded the doors and the back of his neck with his fists.

In order to control his violence (sedation failing), it was necessary to give him almost daily shock treatments. Thus, up to Nov. 2, 1942 a total of 94 convulsions were induced with metrazol, the maximum dose necessary being 13.5 cc. Up to Dec. 16, 1944, he received 152 electric shocks, with an average current of 700 milliamperes for three-tenths second. In addition, he received two treatments of electric narcosis, the last being on Nov. 19, 1942; one was for thirty seconds, at 200 milliamperes and the other for ninety seconds, at 70 milliamperes. The machine used was one of a type constructed by the California Institute of Technology. The first evidence of sustained recovery appeared in September 1944 and was maintained until his parole from the hospital.

A general physical examination on Dec. 26, 1944 showed that his condition was completely normal; the blood pressure was 124 systolic and 76 diastolic. The results of neurologic examination and examination of the eyegrounds were entirely normal. A spinal puncture on Dec. 28, 1944 revealed clear fluid and a pressure of 200 mm. of water; the Wassermann reaction was negative; the reaction for globulin was negative, and there were 5 cells per cubic millimeter. Roentgenograms of the entire spine taken the next day revealed nothing abnormal.

Beginning on December 19, extensive psychologic studies were made. In preface, it should be stated that at the age of 12 years and 10 months the patient

attained an intelligence quotient of 130 on the Stanford Achievement Test; at the age of 14 years and 6 months he had an intelligence quotient of 116 on a general intelligence test.

At this time six tests were made. First, the Otis Employment Test 1, which is a simple verbal test of mental ability, was given. On this test he made a total score of 70, which is the equivalent of the score made by 71 per cent of the general population. Next, the American Council on Education Psychological Examination, 1940 College Edition, was given. This test correlates satisfactorily with progress in college work. On this test he scored a total of 106, with a percentile score of 65. This score is considered to be a satisfactory indication of normal progress in college study. Then the Ohio State University Psychological Examination, Form 21, was given. Here he made a total score of 105 and a percentile rank of 77. This result was definitely higher than that on the previous test, indicating that the absence of a time limit in the Ohio State test was a determining factor. Next, the Bennett Test of Mechanical Comprehension, Form AA, was given. On this test he made a percentile score of 95 as compared with a group of engineering school freshmen, a result which would indicate a high order of ability in perceiving mechanical relationships. Next, he was given the Likert and Quasha Revised Minnesota Paper Form Board Test, Series AA. This is a timed test of spatial perception. Here he made a percentile score of 20 as compared with engineering college seniors, or a percentile score of 55 as compared with students in liberal arts college. The difference in accomplishment between this test and the preceding one is traceable to the necessity of working under the pressure of time. Finally, the Kuder Preference Record Test, Form BB, was given. This test is used in school and college counseling as a preliminary appraisal of fields of vocational interest. Here he showed a heavy weight of interest in scientific and mechanical activities, with a rather low weighting in persuasive, musical and clerical activities.

From the results of these tests, it was concluded that the patient was intellectually capable of a slightly better than average level of college scholarship, and, further, that he was of superior ability as compared with the total population and had undergone no greater change in intellectual capacity than is normal with increasing age. Qualitatively, he showed only an inability to do well in a speed test. With regard to the latter, however, it might be mentioned that relatives of the patient claim that now he is more alert and quicker than ever before.

The mental examination in January 1945 disclosed nothing of importance in the family history. His birth and early development were normal. In the sexual sphere, he admitted the practice of fellatio at the age of 10 for a period of one year and of intercourse in ano at 20 years of age. He masturbated as often as three times daily. However, he had had normal heterosexual experiences. He claimed that he had never married because of the lack of opportunity and his poor financial condition. He denied alcoholic indulgence. As regards social adaptability, he stated that

he was friendly but self conscious. He enjoyed the company of both sexes, but he was mostly in association with boys and enjoyed male parties. He stated that he was afraid to be too friendly with persons below his social standards. His other adjustments appeared to be within normal limits, and his medical and surgical history was essentially without significance. No gross intellectual or emotional impairment was elicited.

The conclusion based on an electroencephalographic examination, made on Feb. 1, 1945, was borderline cerebral dysrhythmia without localization.

On Feb. 7, 1945 the patient was paroled, and it is understood that he is now making a satisfactory social and occupational adjustment.

CONCLUSION

The benefits derived from convulsion therapy usually far outweigh the possible complications which may occur. It appears from this case that convulsive shock therapy does not lead to intellectual, emotional or physical deterioration.

Dr. Clemson Marsh, White Memorial Hospital, Los Angeles, made the electroencephalographic study, and Mr. J. W. McDaniel, psychologist, of the San Bernardino Valley Junior College, made the psychologic tests.

3239 H Street.

News and Comment

POSTGRADUATE COURSE IN PSYCHIATRY, MCGILL UNIVERSITY

McGill University has announced a four year post-graduate course in psychiatry, leading to a diploma. The prerequisites for this course are a degree from an approved medical school or college, a general internship of one year's duration and satisfactory personal qualifications.

The course is designed to prepare men primarily for work in teaching, research, community psychiatry and consultation. It includes experience in the Allan Memorial Institute of Psychiatry and in the wards and the outpatient departments of the Royal Victoria Hospital. Part of the time is spent in dealing with long term cases in designated mental hospitals, in neurology and neuropathology and in community psychiatry.

MEDICAL CORPS, NINTH SERVICE COMMAND

A conference on neuropsychiatry by members of the Medical Corps of the Ninth Service Command was held at the Bushnell General Hospital, Brigham City, Utah, on Oct. 1 and 2, 1945.

Col. Lauren H. Smith, consultant in neuropsychiatry of the Ninth Service Command, was in the chair.

The meeting was opened by Brig. Gen. Robert M. Hardaway and Brig. Gen. William C. Menninger. The following papers were presented: General Therapeutic Program in an Army General Hospital, Col. Olin B. Chamberlain; Convulsive Shock Therapy in an Army General Hospital, Lieut. Col. Mark Zeifert; Subconvulsive Insulin Shock Therapy, Major Daniel J. Sullivan; Psychotherapy of the Neurologically Disabled Soldier, Lieut. Col. Edward O. Harper and Capt. Edward C. Clark; Emotional Adjustment of Newly Blinded Soldiers, Lieut. Col. H. D. Shapiro; Reeducation of Aphasic Patients, Lieut. Joseph M. Wepman; Treatment of Psychiatric Patients in an Army Regional Hospital, Major Arthur M. Kasey Jr. and Capt. C. E. Stanfield.

NEUROPSYCHIATRIC INSTITUTE OF CLEVELAND

The Neuropsychiatric Institute of Cleveland has been established at 10528 Park Lane, Cleveland 6. Its aim is to provide clinical facilities for diagnosis and treatment of patients, as well as a research and teaching program. Seminars in neuropsychiatry have been es-

tablished for physicians of the Veterans Administration in this region and for local practicing doctors.

The staff of the Neuropsychiatric Institute at present consists of Dr. J. L. Fetterman, director; Dr. M. D. Friedman, associate director; Dr. A. A. Weil, research psychiatrist, and Dr. Evelyn Katz, clinical psychologist.

UNIVERSITY OF CALIFORNIA COURSE IN PSYCHIATRY

The University of California extension division, in cooperation with the Division of Psychiatry, University of California Medical School, announces a twelve weeks' refresher course in psychiatry for physicians returning from military service, starting Jan. 7, 1946, at the Langley Porter Clinic, San Francisco Campus, University of California Medical School.

Instruction will be given under the direction of Dr. Karl M. Bowman, professor of psychiatry, of the division of psychiatry of the University of California Medical School, with the assistance of staff members from other divisions of the medical school. Subjects to be covered will include general psychiatry, functional and organic psychoses, psychoneuroses, therapy, psychosomatic problems, neuroanatomy, clinical neurology, neuropathology, roentgenographic diagnosis and other related topics.

Registration is open to graduates of approved medical schools with nine months' general internship. Preference will be given to applicants with training in psychiatry, to those preparing for examination by the American Board of Psychiatry and Neurology, to graduates of the University of California Medical School and to legal residents of the state of California.

The fee for the course will be \$200, payable in advance.

Immediate application for registration is recommended, because of the limited enrolment which can be accommodated. Application should be made by letter containing the following information: (1) place of legal residence; (2) medical school attended and date of graduation; (3) experience and training, with special details regarding psychiatric training, and (4) record of military service. Address applications to: University Extension, University of California, 540 Powell Street, San Francisco 2. Check or money order to cover enrolment fee and made payable to the Regents of the University of California should also be enclosed, unless registration is under G. I. Bill of Rights, in which case only application is necessary. Further details regarding the course may be obtained from the above address.

Obituaries

PÍO DEL RÍO-HORTEGA, M.D.
1882-1945

Pío del Río-Hortega¹ was born in the Spanish town of Valladolid, in the district of Old Castile, on May 5, 1882. His father, del Río, inherited a castle in the nearby countryside, but it had long ago fallen into ruin; and so the boy went to school in the city and his family occupied a house there which formed one whole side of the principal plaza.

His boyhood was apparently a happy one, and he enjoyed its recollection. He often recalled the bull baitings which were staged in the plaza once each year, while townspeople, dressed in their best, watched from balconies. He liked to tell how the young bull was played but never harmed and how an energetic beast once charged out of the square and up a stairway that led into his own house. He was wont to contrast this harmless sport with the brutality of the professional bull fight, which he disliked and would never witness.

He entered the University of Valladolid and graduated in medicine, after which he began to practice; but this did not satisfy his keen, restless mind. He returned to the histologic laboratory and later obtained a traveling fellowship, which took him to Paris and also for a few weeks to London. Then he returned to Spain and journeyed up to Madrid, anxious to work with Spain's most brilliant scientist, Don Santiago Ramón y Cajal, who was then at the height of his renown. Cajal was a national figure of much importance because of the recognition that had come to him from abroad for his scientific work and because of his ability as a writer, artist and leader of thought; a rugged sort of man of peasant stock, a man looked on by his countrymen as the prophet of a new order.

Hortega was a Spaniard of a different type—shy, sensitive, aristocratic, proud, and yet he resembled the master in that he was an artist and an eager perfectionist. He was accepted, and Cajal set him to work for a time with Achúcarro and later took them both into his own, third story laboratory with his other disciples, Tello, Lafora, de Castro and others.

At the time of Hortega's arrival, Cajal had turned from his work on neurons and neuron connections, which had brought him a share in the

Nobel prize of 1906, to the study of neuroglia. In 1913 he had published his monumental contribution on the astrocyte.² The work was based on a new method of metallic impregnation (gold chloride-mercury bichloride method). But in this study Cajal had pointed out that there remained a large group of small cells in the central nervous system that did not seem to be neurons but that were, nevertheless, resistant to staining by any existing neuroglial method. To these cells Cajal had given the title of the "third element" in the central nervous system.

Hortega began his work by using the standard laboratory methods and learned microscopic drawing from the master. Outside the laboratory, he occasionally turned his attention to painting of a classic type, as shown by a full length picture of one of the saints, done in the Spanish style of "sacred art," which later hung in his home.

After a year or two he turned his attention to Cajal's third element, and, encouraged by Achúcarro, he began to experiment with various techniques. Thus, in 1916 and 1917 appeared his first publications on neuroglia studied by Cajal's methods. Then, in 1918, he described a new method of his own, that of ammoniacal silver carbonate. In 1919 he showed that by this method he could stain the third element, which he divided into two groups.³ One of these groups he named microglia and the other, which he described fully in 1921, he named oligodendroglia.⁴

It now became clear that microglial cells truly represented a third element: They were of mesodermal origin, corresponding to the reticuloendothelial cells found elsewhere in the body, cells which were readily transformed into mobile macrophages by destructive processes in the surrounding brain.⁵ The oligodendroglial cells, on the other hand, were in reality smaller neu-

2. Ramón y Cajal, S.: *Trab. d. lab. de invest. biol. de la Univ. de Madrid* 11:219, 1913.

3. del Río-Hortega, P.: *Trab. d. lab. de invest. biol. de la Univ. de Madrid* 14:269, 1919.

4. del Río-Hortega, P.: *Bol. real Soc. españ. de hist. nat.*, January 1921.

5. del Río-Hortega, P.: *Microglia*, in Penfield, W.: *Cytology and Cellular Pathology of the Nervous System*, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 483.

1. Pío decided early to use his father's and mother's names joined by a hyphen, instead of separately, as is the custom in Spain.

roglial cells which seemed to serve as neuron satellites.⁶

Del Río-Hortega now worked under the pressure of a great excitement. He made elaborate black and white drawings of these cytologic discoveries, using paint in the manner of the Spanish school, as he had been taught. He fell into the habit of taking his drawing with him to the Spiedum Coffee House, where his own group of friends met in a *tertulia* each evening at 10 o'clock. Often, after the string quartet had stopped its music and the friends had drifted off to

formed between them at this time which was to last for thirty years.

After this startling discovery was announced by the youngest member of the "school," all did not go well in the laboratory. Jealousy of the brilliant newcomer crept in. Cajal himself was curiously loathe to accept the fact that the last of the interstitial cells of the central nervous system could have yielded their cytologic secrets to a new method.

And so it came about that while the Spanish government was taking steps to build a larger



PÍO DEL RÍO-HORTEGA, M.D.
1882-1945

their homes, he would carry on with his drawing in the cool of the night, elaborating the day's sketch in the company only of his friend Gómez until closing time at 2 o'clock in the morning.

Gómez, or Nicolas Gómez y del Moral, was a business man more interested in things artistic and in the amenities of life than in either science or business. A good-humored gentleman, of a type rarely found outside Spain, he was filled with admiration for the brilliance of Hortega and became his champion. Thus a friendship was

and more elaborate institute, to be named for Cajal, his most brilliant pupil left his group. But nevertheless, it was Cajal who used his influence to establish Hortega in a new laboratory at the Students' Residence (which they referred to as the Residencia), on the outskirts of Madrid. This laboratory and an adjacent laboratory of physiology, of which Prof. Juan Negrin⁷ was

New York, Paul B. Hoeber, Inc., 1932, vol. 2, chap. 9, p. 423.

7. Negrin later became premier of the Spanish Republic and leader of the ill fated republican forces during the civil war.

6. del Río-Hortega, P.: Neuroglia, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System,

directo
lished
search
Studen
Prado
Sacris
labora
twelve

It w
graph
his pu
man,
of sp
stood
his th
showe
hands
There
ment
techni
his ha
with r
turne
and m
or no
and o

At
cover
appar
the ne
Bailey
Da F
many

Ho
patho
ten ye
Instit
the U
work
than
signifi
ings
nume
cytol

At
same
older
his f
great
appa
betw
to fe
thoug
fierc

8.
9.
which
reman
10.

director, were supported by a committee⁸ established to promote progressive education and research and to provide traveling fellowships. Students flocked to Hortaega's laboratory: Prados, Asúa, Ortiz Picón, Costero, Calandre, Sacristán and others, and the single room of the laboratory was filled all day long with six to twelve workers.

It was about this time (1924) that the photograph reproduced here was taken. Don Pío, as his pupils respectfully called him, was a small man, dapper, alert, quick of movement, rapid of speech, highstrung, fastidious. When he stood by one of the El Greco paintings in Toledo, his thin, aquiline profile and slender fingers showed a striking resemblance to the faces and hands of the nobles of the court of Philip II.⁹ There was in his laboratory a feeling of excitement about histology. Every man was his own technician and took great pride in demonstrating his handiwork. General discussion had to do with microscopic preparations, while "small talk" turned on Spanish art and architecture, ancient and modern, instead of baseball, cricket, politics or nocturnal conviviality, as in other laboratories and other lands.

At this time the application of Hortaega's discoveries to pathologic problems was becoming apparent in clinical centers, as was shown during the next few years in the publications of Percival Bailey, Cushing and Cone, in the United States; Da Fano, in England; Metz and Spatz, in Germany; Rezza, in Italy, and numerous others.

Hortaega shortly turned his own attention to pathology,¹⁰ at the Madrid General Hospital and ten years later had become director of the Cancer Institute in the newly built University City of the University of Madrid. However, his own work on pathologic subjects is of less importance than his contributions to pure histology, and it is significant that he continued to spend his mornings at the Residencia, where he worked with numerous students on normal and experimental cytology.

At that time, in 1934, he seemed much the same as he had ten years before, although he was older and was now an acknowledged leader in his field. Cajal, on the other hand, had aged greatly and had become deaf and infirm. It was apparent, however, that there was no bitterness between these two great histologists; each seemed to feel pride in the other's accomplishments, although their friends were conscious of a sort of fierce rivalry. Never did Hortaega refer to his

master except in terms of greatest admiration. International recognition might well have come to the pupil for his brilliant contributions, as it had to the master, if dreadful civil war had not come upon Spain.

This time, that preceded the outbreak of civil war, was for Spain a time of renaissance in art, music, science and progressive education—a renaissance eventually destroyed by Fascist might. During the siege of Madrid, Hortaega remained in the city. He witnessed the complete destruction of the Cancer Institute by shell fire. His books were used to build bulwarks against snipers, and the laboratory, with its histologic treasures and microscopes, gradually dissolved in the devastation of "no man's land."

But he was neither a soldier nor a politician, and he turned back to his microscope for consolation. There followed a period in Valencia with his first pupil, Miguel Prados, when he resumed his studies for a little time. Shortly, however, he was sent to Paris by the republican Government with his friend Gómez. On reaching Paris, in 1937, this "Jonathan and David" showed the effect of the war years all too plainly. Hortaega was very thin, his hair graying, his movements more nervous than ever; and he seemed to have grown a little smaller. Gómez was gaunt from privation. His clothes hung on him in folds, but this man, who had been wont to wear a cloak of an evening with the air of a grandee, was still debonair and able to laugh in the face of adversity. Hortaega worked then for about a year in the laboratory of the neurosurgical clinic of Prof. Clovis Vincent, at La Pitié Hospital.

After Paris, there followed a few years in Oxford. Thanks to Prof. Hugh Cairns, a laboratory was fitted up for him in the Radcliffe Infirmary that resembled his first laboratory at the Students' Residence, in Madrid. Here he had ample pathologic material for study and was associated with a kindred histopathologist, Dr. Dorothy Russell. Gómez made a gallant effort to create a congenial atmosphere in this strange land, but the tragedy of Spain weighed heavily on Hortaega; he found the English language impossible to master, and he missed the Spanish way of life.

And so, when he was offered a haven in Argentina and a university laboratory, they sailed for Buenos Aires, where for a time students again gathered about his microscope. He founded a new journal—*Archivos de anatomía normal y patológica*. But, again, political hostility interfered with the promised development of his laboratory; ill health came, and on June 1, 1945, Pío del Río-Hortaega died.

8. Junta para ampliación de estudios e investigaciones.

9. The portrayal of the burial of the Count of Orgaz, which covered one wall of a church in Toledo, is a remarkable record of these Castilian courtiers.

10. Arch. españ. de oncol. 1:477, 1930; 2:411, 1932.

In an unpublished address¹¹ on "Art and Artifice in the Science of Histology," Hortega has put into words his credo. It explains the excitement and pleasure that he always showed while working at his microscope. There was for him romance and art, as well as discovery, in the land beyond the lenses.

Histology is a respectable and respected science. It serves, among many other purposes of importance, to give prestige to the rest of medicine. In all proper publications, histology is given the chief place. At the banquet of medicine it is the guest of honor, who eats little—aloof, mysterious—to whom all listen, yet whom very few understand. . . .

This science, which illuminates the structure of cells and tissues, has two facets: one cold, factual, static, which reflects only the metaphysical; the other pleasing and dynamic, which brings to light the art of the subject.

I have to confess that if there were only the first aspect, with its abstruse ideas, its chimeras and its pedantic pronouncements, I could not be a histologist. Further, I firmly believe that in order to be a good histologist it is necessary to have the soul of an artist and to possess the sense of true romance. . . .

11. Translated by one of Hortega's younger pupils, Dr. William Gibson, who has allowed me to make the accompanying quotations.

For my own part I confess that I do not know what made me become a histologist, whether it was keen ambition, a fervent desire (nearly always disappointed) to see that which no one else has seen or simply an incessant yearning to see for myself the marvels of natural structure, stripped of its disguise by means of technical artifice. . . .

Finally, he added:

. . . The emotion which is associated with a discovery, small though it may be, generously repays the investigator for his finished labor.

Pío del Río-Hortega contributed an important chapter to knowledge of the structure of the central nervous system. He threw a clear light on the form and function of the interstitial cells. He provided the fundamental cytologic descriptions which were needed in the classification of tumors of the brain and spinal cord. He simplified and clarified the study of cytogenesis and pathologic alterations within the brain. Outside the field of cytology his influence was felt first in neurosurgery, but his work has had an influence on the study of neurologic and psychiatric disease in general which will grow in importance as the years pass.

WILDER PENFIELD, M.D.

EMBRYO
TH
DER
EM

The
late ga
tema f
as wel
ectode
only a

Ecto
and su
horny
when t
notoch
trula
but ho
as we
the ea
depend
ectode
sucker
gradua
is inde

Inte
are fo
ventra
orienta
blaste
lip me
periton

PHAS
TE
OS
Zo

The
of lan
opacu
ble st
and a
resect
nerv
to six

The
for (c
starts
(b) t
regen
ence
differ
genes

The
specif
portar
morph

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

EMBRYONIC GRAFTS IN REGENERATING TISSUE: III.

THE DEVELOPMENT OF DORSAL AND VENTRAL ECTODERM OF *RANA PIPIENS* GASTRULAE. HENRY S. EMERSON, J. Exper. Zool. **97**:1 (Oct.) 1944.

The middle of the presumptive neural plate of the late gastrula that has been transplanted into the blastema forms some epidermis and epidermal derivatives, as well as brain and eyes. In these transplants the ectoderm has been underlaid by chorda mesoderm for only a short time.

Ectoderm from the early gastrula forms epidermis and suckers, and occasionally nerve tissue and cartilage; horny jaws develop in about half the cases, especially when there is contact of the graft with the regenerating notochord of the host. Ectoderm from the middle gastrula develops like ectoderm from the early gastrula, but horny jaws are always formed, and often nasal sacs as well. Nasal sac competence must occur between the early and the middle gastrula stage and does not depend on the action of the archenteron roof. Ventral ectoderm of the late gastrula forms only epidermis, suckers and horny jaws. These results indicate a gradual chemodifferentiation within the ectoderm which is independent of the action of the chorda mesoderm.

Intestinal tubes with the mucosa toward the lumens are formed from the endodermal substratum of the ventral ectoderm from the late gastrula. The normal orientation of the gut mucosa is due to the surrounding blastema mesenchyme. As was expected, the ventral lip mesoderm forms celom, with visceral and parietal peritoneum and sometimes mesenteries.

REID, Boston.

PHASES IN REGENERATION OF THE URODELE LIMB AND THEIR DEPENDENCE UPON THE NERVOUS SYSTEM. OSCAR E. SCHOTTÉ and ELMER G. BUTLER, J. Exper. Zool. **97**:95 (Nov.) 1944.

The influence of nerves on regeneration of the limb of larvae of *Amblystoma punctatum* and *Amblystoma opacum* was studied in 252 larvae. To obtain comparable stages of regenerating limbs, temperature conditions and age of larvae were carefully controlled. Repeated resection of the brachial plexus insured permanent nervelessness of the limbs. Denervation occurred two to sixteen days after amputation.

The presence of nerves was found to be necessary for (a) the whole of the dedifferentiative phase which starts regeneration and establishes the blastema, and (b) the transformation of the young blastema into a regenerate with morphogenic determination. The presence of nerves was found unnecessary for growth and differentiation of the regenerate (phase of morphogenesis).

The nervous system is an important agent only for specifically regenerative activities; it is no more important for morphogenesis during regeneration than for morphogenesis in development of embryonic limbs.

REID, Boston.

THE BRAIN OF *DROSOPHILA MELANOGASTER*. MAXWELL E. POWER, J. Morphol. **72**:517 (May) 1943.

The finer anatomy of the brain of the wild type *Drosophila melanogaster* (Oregon R) was studied, using sectioned material stained by a modification of the Bodian silver impregnation technic.

The brain is a laterally elongate, compact body in which the protocerebrum, deutocerebrum and tritocerebrum are fused together. It has a cellular cortex and a fibrous core, which is organized into glomeruli: (a) the central complex, (b) a pair of corpora pedunculata, (c) the protocerebral bridge, (d) a pair of antennal glomeruli and (e) three pairs of optic glomeruli. These are connected with each other and with the general brain by tracts and commissures.

The central complex contains four glomeruli and is an association center, receiving fibers from several parts of the brain.

The corpora pedunculata, or mushroom bodies, are on either side of the central complex, and each is composed of three stalks, extending in different planes of orientation. These bodies are less well developed than those in other orders of insects.

The protocerebral bridge is a transverse cylinder located in the dorsoposterior portion of the brain. The bridge is an association center, being connected with the central complex, the optic tubercles, the antennal glomeruli and the general brain.

The antennal glomeruli (deutocerebrum) are located anteriorly and are connected by commissures above the esophagus. The largest fiber bundles are the olfactoria globularis tracts and the pair of large antennal nerves which are connected with the antennae.

The lateral portions of the brain are the optic lobes, each of which contains three optic glomeruli. The external glomerulus is separated from the middle glomerulus by the external chiasm (centripetal visual fibers). The internal glomerulus has an anterior and a posterior portion, which are connected with each other and with the middle glomerulus by the fibers of the internal chiasm. All connections between the optical system and the central portions of the brain are by way of the internal glomeruli. The middle glomeruli are connected with each other by a special commissure. There are five major tracts placing the inner glomeruli in communication with other parts of the brain.

The opposite sides of the protocerebrum proper are connected with each other by three major commissures. Extending through the protocerebrum, but belonging to the deutocerebrum, is the pair of olfactoria globularis tracts from the antennal glomeruli.

In addition, there are two median, unpaired tracts, each of which extends dorsoventrally and enters the subesophageal mass. One of these, the ocellar stalk, extends into the thoracic nervous center.

The cellular cortex is composed of cells of different sizes and shapes which are arranged on the surface of the brain with precise bilateral symmetry.

REID, Boston.

THE AFFERENT PATH OF THE PUPILODILATOR REFLEX IN THE CAT. A. J. HARRIS, R. HODES and H. W. MAGOUN, *J. Neurophysiol.* 7:231 (July) 1944.

Harris, Hodes and Magoun studied the dilatation of the pupil resulting from stimulation of the sciatic, splanchnic and trigeminal nerves and observed the responses to such stimulation after various lesions of the spinal cord and brain. The authors found that the reflex was mediated at the level of the midbrain, since the destruction of the brain above the oculomotor nucleus did not impair the response. A pathway common to all types of stimuli administered ascends through the lateral funiculus of the cord and the reticular formation of the medulla, lies in a paramedian position in the dorsal pontile tegmentum and ascends through the midbrain in or near the central gray matter. This pathway is distinct from the lateral spinothalamic tract.

FORSTER, Philadelphia.

Physiology and Biochemistry

VARIATION IN CIRCULATORY AND RESPIRATORY RESPONSES TO CAROTID SINUS STIMULATION IN MAN. M. GALDSTON, R. GOLDSTEIN and J. M. STEELE, *Am. Heart J.* 26:213 (Aug.) 1943.

Galdston and his associates review the history of research on stimulation of the carotid sinus, giving particular attention to the investigations of Weiss and his co-workers, who distinguished three types of syncope resulting from such stimulation. The first, in which syncope is accompanied with definite slowing of the heart rate or asystole and a consequent fall in arterial pressure, is designated the "vagal type"; the second, in which a pronounced fall in arterial pressure occurs without significant slowing of the heart, the "depressor type," and the third, in which there is syncope without either slowing of the heart or fall in arterial pressure, the "cerebral type." The authors studied the relationships, in point of time, of arterial pressure, pulse rate, venous pressure, respiration and onset of syncope and convulsions. One hundred persons were examined, 26 of whom presented a sensitive carotid sinus reflex. Of these, 17 regularly had convulsive seizures on stimulation of the carotid sinus. The common circulatory response in the 17 persons was slowing of the heart and asystole (vagal response), with a fall in arterial pressure (depressor response). A pure vagal response was next most common. A pure depressor response was not observed except when the patient was under the influence of atropine. Paredrine hydrobromide aqueous prevented to a large degree the depressor responses. Two patients had convulsions without significant circulatory change (cerebral type). In 3 other patients syncope and convulsions persisted when circulatory changes were inhibited by the administration of atropine or paredrine hydrobromide. Hyperpnea is the regular respiratory response to digital pressure in the region of the carotid sinus. Its occurrence is independent of the circulatory response. It is independent of age or sex. It is not prevented by barbiturate anesthesia, but local infiltration of the region about the carotid sinus and carotid body with procaine hydrochloride abolishes it. Prolonged stimulation is often followed by a phasic type of respiration similar to Cheyne-Stokes breathing. Evidence is presented that hyperpnea after pressure on the neck in the region of the carotid sinus in man may be caused by a disturbance of the blood supply to the carotid body rather than by mechanical stimulation of the carotid sinus.

J. A. M. A.

THE EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRIN AND ANGIOTONIN BEFORE AND AFTER THE PRODUCTION OF NEUROGENIC HYPERTENSION. CAROLINE BEDELL THOMAS and ROSS L. MCLEAN, *Bull. Johns Hopkins Hosp.* 75:319 (Nov.) 1944.

Thomas and McLean report on the effect of intravenous injections of epinephrine and angiotonin on 3 unanesthetized dogs before section of the moderator nerve and when hypertension was present. The observations show that pressor responses to epinephrine and angiotonin are not significantly altered by the induction of neurogenic hypertension. Angiotonin produces a marked cardiac acceleration in the hypertensive animal, whereas it slows the cardiac rate slightly when the dog is in the normal state. Epinephrine has a similar, but less pronounced, effect on the heart rate.

These data indicate that while peripheral vasoconstrictor activity may be increased in the case of neurogenic hypertension, vasoconstrictor tone is not sufficiently great to interfere with the action of either sympathicomimetic or humoral vasoconstrictor substances. Angiotonin stimulates the cardioaccelerator mechanism, but this effect is normally masked by the moderator reflexes.

GUTTMAN, Philadelphia.

LACTIC ACID OXIDATION QUOTIENT IN MINCED BRAIN OF NORMAL AND AVITAMINOTIC CHICKEN. P. E. GALVÃO, J. PEREIRA and J. P. LIMONGI, *J. Biol. Chem.* 157:667, 1945.

Few data are available on the quotient of lactic acid oxidation, i. e., lactic acid removed/lactic acid oxidized, in the central nervous system. Determination of the quotient of lactic acid oxidation in the brain of birds seemed particularly interesting because these animals show a disturbance in the oxidation of lactic acid in specific regions of the central nervous system. With birds exhibiting pronounced symptoms of B₁ avitaminosis, the decreased oxidation of the lactic acid formerly noted for the brain stem was not accompanied with an impaired removal of lactate. The quotient of lactic acid oxidation, therefore, increased. Addition of thiamine hydrochloride produced partial restoration of the oxidation of lactate without significant influence on the removal of lactate; the quotient, consequently, tended toward normal. In the present experiments the nerve tissue was finely minced. This treatment brought about results substantially different from those obtained with thoroughly ground tissue used in the previous experiments. In the brain stem of avitaminotic chickens a great diminution of extra oxygen was accompanied with a considerable, though smaller, reduction in removal of lactate; consequently, the oxidation quotient tended to rise. Addition of thiamine hydrochloride, besides promoting the extra oxygen uptake, increased removal of lactate. No differences were found between normal cerebrum and the cerebrum of birds with B₁ avitaminosis.

PAGE, Cleveland.

FUNCTIONAL DIFFERENTIATION IN EMBRYONIC DEVELOPMENT: I. CHOLINESTERASE ACTIVITY OF INDUCED NEURAL STRUCTURES IN AMBLYSTOMA PUNCTATUM. EDGAR J. BOELL and SHIH-CHANG SHEN, *J. Exper. Zool.* 97:21 (Oct.) 1944.

Boell and Shen determined the cholinesterase content of various tissues in developing embryos of *Amblystoma punctatum* with a modified ultramicromanometric technique. At the period of the closing of the neural folds there was a significant localization of cholinesterase in the nervous system, as compared with the amount in the ectoderm. The concentration of cholinesterase be-

came progressively greater as the nervous system differentiated.

The cholinesterase activity of secondary, induced, neural structures, produced by the action of implanted chorda mesoderm on competent ectoderm, is of the same order of magnitude as that of the primary neural tissues of the host. Ectoderm which has not received the stimulus of the inductor has a much lower cholinesterase value.

Apparently, induction, in addition to causing the development of distinct morphologic changes, stimulates the induced tissue to develop the characteristic biochemical machinery of normal nerve tissue. The authors suggest that the cholinesterase content of secondary, induced, neural structures may be considered as a measure of their potential or incipient functional differentiation.

REID, Boston.

LIMB PARAMETERS AND REGRESSION RATES IN DENERVATED AMPUTATED LIMBS OF URODELE LARVAE. OSCAR E. SCHOTTÉ and ALEXANDER G. KARCZMAR, *J. Exper. Zool.* **97**:43 (Oct.) 1944.

The regression in denervated amputated limbs of *Amblystoma* and *Triturus* larvae (18 to 48 mm.) was studied under constant temperature conditions (16 and 20 C.). Regression rates were obtained from measurements of camera lucida drawings made at regular intervals and expressed in microns per hour for the absolute individual regression rate, or referred to the initial length of the stump and expressed in per cent per hour for the relative individual regression rate. Regression rates presented remarkable fluctuations, which were correlated with the dimensions of the regressing limbs.

Comparison of relative individual regression rates in long and in short limbs showed that long limbs exhibit slower regression rates than short limbs and that the rates are independent of anatomic levels.

The general trend of regression rates is determined by the activities of the dedifferentiation phase, while the variability of these rates is conditioned by the volumes of limb material available. Thick limbs regress with slow rates; thin limbs, with high rates; medium-sized limbs, with average rates. Since the volume removed is directly proportional to the cross section area of the limb, the cross section area (width parameter) of the limb appears to be the controlling agent of the disposal phase. This is especially striking in thin limbs.

The heterogeneity of histologic structures in denervated amputated limbs influences the two phases of regression. Bone, cartilage and tendons resist the regression process more than do the soft tissues of the limb.

At present the regression effect appears to be the result of an interplay of three factors: (a) availability of materials, determined by the limb dimensions and subject to the activities of the dedifferentiation phase; (b) a limiting factor, the disposal phase, controlled by the width parameter of the limb, and (c) a modifying factor, determined by the biochemical and biophysical nature of the regressing tissues and conditioned by the physiologic age of the denervated amputated limb.

REID, Boston.

THE FORMATION OF ACETYLCHOLINE: A NEW ENZYME: "CHOLINE ACETYLASE." D. NACHMANSOHN and A. L. MACHADO, *J. Neurophysiol.* **6**:397 (Sept.-Nov.) 1943.

Nachmansohn and Machado extracted an enzyme which forms acetylcholine from the brains of various

species and from the electric organ of *Electrophorus electricus*. This enzyme they named choline acetylase. The formation of acetylcholine by this enzyme occurs only in the presence of adenosine triphosphate. Fluoride enhances the formation of acetylcholine. According to Ochoa, fluoride inhibits adenosine triphosphate but not the transfer of phosphate to a phosphate acceptor. Potassium and ammonium ions within certain concentrations do not affect the enzyme, while copper, iodoacetic acid and iodine strongly inhibit the activity of the enzyme.

FORSTER, Philadelphia.

AN ANALYSIS OF THE VARIABILITY OF SPINAL REFLEX THRESHOLDS. J. S. DENSLOW, *J. Neurophysiol.* **7**:207 (July) 1944.

Denslow studied the thresholds of reflex muscle contraction on applying moving pressure stimuli to the spinous processes. The thresholds were found to be relatively constant in a given subject, with wide variations in thresholds in different subjects and with variations from segment to segment, and even from side to side, in the same subject. These differences may be due to (1) change in environment of deep pressure or stretch receptors in areas of medium and high threshold levels and to a change in that of other endings in low threshold areas and (2) to an imbalance of excitatory-inhibitory influences, such as may occur in an enduring subliminal central excitatory state. Denslow found the mean threshold to be slightly higher on the left side of the body than on the right. He concludes that in the absence of organic disease, thresholds for reflex muscle contraction might provide a neurologic index of the efficiency of the organism in coping with mechanical weaknesses and with environmental stresses.

FORSTER, Philadelphia.

PARASYMPATHETIC REGULATION OF HIGH POTENTIAL IN THE ELECTROENCEPHALOGRAM. CHESTER W. DARROW, JOHN R. GREEN, EDWARD W. DAVIS and HUGH W. GAROL, *J. Neurophysiol.* **7**:217 (July) 1944.

Darrow, Green, Davis and Garol sectioned the facial nerves of cats so as to interrupt the parasympathetic pathways to the pial blood vessels. The animals were curarized and placed under artificial respiration. Under these conditions hyperventilation produced high potential, slow and spiked activity of the cerebral cortex. These alterations of potential could be abolished by stimulation of the peripheral cut end of the facial nerve or by the intravenous administration of physostigmine, whereas the application of atropine enhanced the response. The authors conclude that a parasympathetic influence on the electrical activity of the brain has been demonstrated and that a cholinergic influence on cerebral metabolism and circulation is implied. The homeostatic regulation of cerebral circulation is probably through a supplemental relationship between acetylcholine and carbon dioxide.

FORSTER, Philadelphia.

CHANGES OF WEIGHT AND NEUROMUSCULAR TRANSMISSION IN MUSCLES OF IMMOBILIZED JOINTS. P. THOMSEN and J. V. LUCCO, *J. Neurophysiol.* **7**:245 (July) 1944.

Thomsen and Lucco studied the effects of fixation of the tibiotarsal joint on the neuromuscular synapse and the weight of the soleus and tibialis anticus muscles of cats. Fixation of the joint was in hyperextension, in hyperflexion or in midposition. Alterations in neuro-

muscular transmission after these fixations were the same as after tenotomy. Moreover, the immobilized muscles, like tenotomized muscles, were less sensitive to curare. Fixation in hyperflexion up to fourteen days resulted in an increase in the weight of the soleus and a decrease in the weight of the tibialis, while the converse was obtained with fixation in hyperextension. The authors conclude that in immobilization, as in tenotomy, the abnormal tension to which the muscle is exposed produces the neuromuscular changes through a reflex mechanism.

FORSTER, Philadelphia.

RELATION OF CEREBRAL CORTEX TO SPASTICITY AND FLACCIDITY. W. KEASLEY WELCH and MARGARET A. KENNARD, *J. Neurophysiol.* 7:255 (Sept.) 1944.

Welch and Kennard studied in primates the spasticity and flaccidity resulting from ablations of various areas, either singly or in combination. They confirmed the observations of other investigators on the effects of primary ablations. Removal of area 6, with area 4s, was followed by moderate spastic paresis. Removal of area 4 yielded paresis without spasticity. Removal of the postcentral gyrus resulted in transient flaccidity with some paresis.

Welch and Kennard studied the effects of successive removals of the areas in question. The ablation of areas 4, 4s and 6, either simultaneously or serially, resulted in immediate spastic paresis. When ablations had resulted in spasticity, subsequent ablation of the postcentral gyrus increased the paresis and in monkeys usually increased spasticity, while in chimpanzees the increase of spasticity was definite. Ablation of area 4 and the postcentral gyrus resulted in spasticity. Ablation of any contralateral motor area in addition to a primary lesion causing spasticity increased the spasticity. In the monkey, when the entire hemisphere was ablated, removal of areas 4 and 6 augmented the spasticity and paresis to a greater degree than did ablation of the postcentral gyrus.

FORSTER, Philadelphia.

ACUTE AND CHRONIC PARIETAL LOBE ABLATIONS IN MONKEYS. TALMADGE L. PEELE, *J. Neurophysiol.* 7:269 (Sept.) 1944.

Peele studied the effects of removal of the various cytoarchitectural areas of the parietal lobe of the macaque monkey. Removal of area 3, areas 1 and 2, area 5 or area 7 individually or of areas 1-2, 5 and 7 in combination did not result in paralysis, although the animals were loath to move. Removal of area 3 or of areas 1 and 2 affected the arm and the leg equally, while removal of area 5 affected the leg, and removal of area 7 the arm, particularly. This differential localization was found to be compatible with the distribution of the parietospinal fibers. Hypotonia was consistently present and was more marked proximally. The hypotonia probably accounted for the resting posture of the animals and for the ataxia and slowness of movement. The tendon reflexes exhibited increased threshold, slowness of execution and increased excursion. Tactile and painful stimuli were not as well appreciated after ablations, and localization of stimuli was impossible. Placing and hopping responses were immediately impaired but returned in three weeks, while tactile placing was permanently impaired with postcentral lesions. Muscular atrophy and hyperpathia occurred in 1 animal. The postcentral gyrus appeared essential for recognition of tactile and painful stimuli, and all parietal areas were necessary for localization and discrimination.

FORSTER, Philadelphia.

CEREBRAL METABOLISM IN EXPERIMENTAL HEAD INJURY. E. S. GURDJIAN, J. E. WEBSTER and W. E. STONE, *War Med.* 6:173 (Sept.) 1944.

Gurdjian, Webster and Stone found that the oxygen saturation of arterial blood was frequently increased after experimental head injury in dogs. In a few instances there was a decrease. Variations in respiratory function govern the changes. The cerebral arteriovenous differences in oxygen, carbon dioxide and glucose did not change appreciably as a result of injury to the head. The differences were calculated with blood obtained from the femoral artery and from the sagittal sinus.

Areas of contusion showed increased levels of lactic acid and inorganic phosphate and decreased levels of phosphocreatine and adenosine triphosphate. These changes may be due to a combination of direct injury to the cells and anoxia resulting from vascular damage.

In unbruised areas of the cortex, the chemical constituents studied were frequently entirely normal, even in profoundly injured animals. This was thought to signify that in a great many animals there was no evidence of a generalized disturbance in cerebral oxidations. In a few dogs there was increase in lactic acid in the presence of adequate arterial oxygen. This may represent either a mild degree of local damage or a more widespread disturbance in cerebral oxidative mechanisms in these animals.

Impaired oxidative mechanisms may occur in localized areas of the cortex without significant changes in cerebral arteriovenous differences in oxygen, carbon dioxide or glucose.

Improvement occurs in the oxidative processes in areas of contusion during a two day recovery period, as evidenced by return toward normal levels of the chemical constituents studied.

Although administration of oxygen induces no striking acceleration of recovery processes, the results seem to indicate a trend toward better recovery with high intake of oxygen.

PEARSON, Philadelphia.

A COMPARISON OF ALTITUDE AND EXERCISE WITH RESPECT TO DECOMPRESSION SICKNESS. S. F. COOK, O. L. WILLIAMS, W. R. LYONS and J. H. LAWRENCE, *War Med.* 6:182 (Sept.) 1944.

Four groups of healthy young men (aged 18 to 20) were given two chamber tests each. One group performed a standard exercise at 30,000 feet (9,150 meters) every five minutes for ninety minutes; the exercise consisting of ten 9 inch (23 cm.) step-ups in thirty seconds. The second group performed the same exercise every two and one-half minutes at the same altitude. The third group performed the standard exercise every five minutes at 38,000 feet (11,500 meters), and the fourth group performed the exercise every two and one-half minutes at 38,000 feet. The following criteria were used in comparing the bends-inducing effect of the four sets of conditions: the per cent incidence of symptoms, per cent incapacitation, time of onset of symptoms, time of descent, maximum intensity of symptoms and velocity of development of symptoms. All criteria showed statistically significant differences between the two altitudes with constant exercise. When the altitude was held constant at 30,000 feet, the effect of doubling the frequency of the standard exercise was relatively slight and not of statistical significance in all cases. At 38,000 feet, the effect of increase of exercise was significant with most criteria but was much less pronounced than the effect of changing altitude.

In general increase in the incidence considerably done by me

EXPERIMENTAL

E. A. S. and H.

The author rotating-tilt were produced unselected (rotation of body) wceptibility. with front rotation co effective in produced s were supplied experience.

Optic fi movements of motion tionary of subject.

Typical Their app tative sym ence of tw

Symptom by stimula the cristae

ACUTE H. Med.

A study 27 cases severe ca stant in capillaries gestion. venous an scopic co There w location exception hemorrhha Swelling medulla vacuoles less freq

PYRAMID and C

Liddel pyramida through medulla Unilateral mediate ing, defe ness in up in se (twelve

In general, the conclusion may be drawn that an increase in altitude from 30,000 to 38,000 feet increases the incidence and severity of decompression sickness considerably more than doubling the muscular work done by means of the step-up exercise.

PEARSON, Philadelphia.

EXPERIMENTAL PRODUCTION OF MOTION SICKNESS.

E. A. SPIEGEL, M. J. OPPENHEIMER, G. C. HENNY and H. T. WYCIS, *War Med.* **6**:283 (Nov.) 1944.

The authors tested a number of medical students on a rotating-tilting machine. Symptoms of motion sickness were produced within eight minutes in 75 per cent of unselected subjects. The weaker method of stimulation (rotation combined with sagittal movements of the head or body) was sufficient to reveal a high degree of susceptibility. The stronger stimulation (rotation combined with frontal head movements preceding or succeeding rotation combined with sagittal head movements) was effective in nearly all moderately susceptible persons and produced symptoms even in some of the subjects who were supposedly not susceptible according to previous experience.

Optic fixation of an object that participates in all movements of the head tends to diminish the incidence of motion sickness as compared with the effect of stationary objects of the surroundings watched by the subject.

Typical illusions of spatial orientation were produced. Their appearance was independent of that of the vegetative symptoms of motion sickness, indicating the presence of two rather independent mechanisms.

Symptoms of motion sickness may be elicited not only by stimulation of the maculas but by stimuli acting on the cristae ampullares.

PEARSON, Philadelphia.

ACUTE HIGH ALTITUDE ANOXIA. R. A. KRITZLER, *War Med.* **6**:369 (Dec.) 1944.

A study was made of the observations at necropsy in 27 cases of acute high altitude anoxia. Widespread, severe capillary congestion was found. This was constant in the pulmonary, renal, intestinal and cerebral capillaries. The skeletal muscle failed to reveal congestion. In a high proportion of cases the systemic venous and portal circulations showed gross and microscopic congestion, and the right ventricle was dilated. There was wide individual variation in the incidence, location and amount of edema and hemorrhage. An exception to this was the consistent occurrence of hemorrhage in the thymus and in the middle ears. Swelling of endothelial cells of capillaries of the renal medulla was observed. Fat-free and glycogen-free vacuoles were found in the myocardium and liver and less frequently in cells of other organs.

PEARSON, Philadelphia.

PYRAMIDAL SECTION IN THE CAT. E. G. T. LIDDELL and C. G. PHILLIPS, *Brain* **67**:1, 1944.

Liddell and Phillips studied 34 cats in which the pyramidal tract had been sectioned by an approach through the basioccipital bone with sterile technic. The medulla was subsequently studied in serial sections. Unilateral section of the pyramidal tract produced immediate paresis of the contralateral limbs with scissoring, defective hopping and placing reactions and weakness in flexion of the forepaw. The paresis cleared up in several days, but for the duration of observations (twelve months) placing and hopping were impaired.

The affected hindlimb when unsupported showed a tendency to extension of the solid, long-resisting type without clasp knife effect. This hypertonia of the extensor muscles decreased somewhat from the second to the sixth week. Walking on a horizontal ladder demonstrated the hypertonia well. Pyramidal section which was incomplete or was so extensive that it involved the medial fillet or the olive produced less hypertonia. The knee jerk in the affected extremities was brisk and of extensor type. Section of both pyramidal tracts produced a bilateral picture of the type described for unilateral section. The horizontal ladder test revealed the animal to be immobile.

FORSTER, Philadelphia.

FIBRE INTERACTION IN INJURED OR COMPRESSED REGION OF NERVE. RAGNAR GRANIT, LARS LEKSELL and C. R. SKOGLUND, *Brain* **67**:125, 1944.

Granit, Leksell and Skoglund studied the activity of the sciatic nerve induced by stimuli administered to a component motor or sensory root. To avoid the back response observed by Lloyd, it was necessary completely to denervate the limb. The authors found that under these conditions an electrical response could be elicited when a stimulus was administered to the motor root or to the sensory root and recordings were obtained from the other root. The responses were of greater amplitude when read from the sensory root and the stimulus was applied to the motor root. When recordings were taken from the sciatic nerve and the stimulus was administered to a sensory root, the usual nerve impulse was obtained, followed by a small wave traveling in the opposite direction. This wave was transmitted by an "artificial synapse," due to fiber interaction at the site of section of the sciatic nerve. Like other synapses, this artificial synapse was susceptible to anesthetics and anoxia. Fresh sectioning of a nerve increased the transmission at the artificial synapse for a period of five to ten minutes. Crushing the sciatic nerve with a ligature was as effective as direct sectioning of the nerve. Moderate pressure could produce the same response. In some instances sectioning the popliteal nerve augmented responses begun in the peroneal nerve. The authors concluded that sensory fibers have less capacity to resist stimulation and that since this is particularly true of pain fibers of the so-called C group, this fiber interaction may be of importance in the explanation of causalgia.

FORSTER, Philadelphia.

INVESTIGATIONS ON MUSCLE ATROPHIES ARISING FROM DISUSE AND TENOTOMY. J. C. ECCLES, *J. Physiol.* **103**:253, 1944.

Eccles studied atrophy in inactivated and/or tenotomized muscles in 30 cats. The loss of weight and the response to stimulation were observed. The latter was recorded as the ratio of the maximum tetanic contraction to the weight of the muscle or as the ratio of the maximum tetanic contraction to the maximum twitch contraction. The muscles of the hindlimbs were studied after inactivation through isolation of the lumbar portion of the spinal cord and section of the dorsal roots in the same area. Muscles innervated by the isolated spinal segment generally showed no activity, though fibrillation appeared in some specimens.

It had previously been shown that in such preparations daily tetanization of the sciatic nerve largely prevented loss of weight in the flexor muscles of the ankle joint but was much less effective in the extensor muscles. Because of the greater power of the flexor muscles, they were able to shorten maximally during

stimulation, whereas the extensors were stretched. The influence on muscle atrophy of this difference in length during stimulation was investigated by means of preparations in which appropriate tendons were severed or the ankle joint forcibly held in the desired position. The results of these experiments showed that the greater the length of the muscle during therapeutic stimulation, the better the results with regard to maintenance of weight; however, the reverse was true with regard to the maintenance of response to tetanic stimulation. The results were particularly striking in the flexor muscles but applied in some degree to the extensors. It was found that even under identical mechanical conditions the weight of the flexor muscle was better maintained by daily stimulation of the nerve than was that of the extensor muscle. Consequently, some other unknown factor was involved in the differences in response to therapeutic stimulation of the two groups of muscles.

The influence of shortening on muscle atrophy was further studied by means of tenotomy alone, leaving the nerves intact. Tenotomized muscles undergo maximal shortening and likewise undergo atrophy corresponding to that of disused muscles. The author believes that the atrophy is a result of the excessive shortening. He points out that the most satisfactory condition for preventing atrophy in disused muscle is that in which the muscle shortens against a load during therapeutic stimulation. This conclusion applies both to flexor and to extensor muscles. The one effective treatment for tenotomized muscle is immediate suture of the tendon, since therapeutic stimulation is ineffective in preventing atrophic changes and aggravates the excessive shortening of the muscle.

THOMAS, Philadelphia.

THE INHIBITION OF HISTAMINE RELEASE BY A PITUITARY-ADRENAL MECHANISM. G. UNGAR, *J. Physiol.* **103**:333, 1944.

Previous observations of Gotz and Dragstedt have shown that the blood of normal rabbits when mixed with peptone in vitro releases considerable amounts of histamine. Ungar confirmed these observations in guinea pigs and rats. He found, further, that this reaction was prevented by previous exposure of the animals to sublethal shock due to peptone, trauma or anaphylaxis. The protection against the release of histamine in the presence of peptone can be passively transferred by the injection of serum of previously traumatized animals into the test animals. Apparently, trauma causes the release into the blood of a substance which protects against the release of histamine in the presence of peptone. This protecting agent was absent from the serum of traumatized animals which had been adrenalectomized or hypophysectomized. The author concludes that trauma stimulates the pituitary gland to release a substance which, acting through the adrenal gland, protects against peptone shock. He points out that histamine is probably not the only substance released in the blood in the presence of peptone. Histamine was selected for study because of the ease with which it can be estimated quantitatively.

THOMAS, Philadelphia.

Neuropathology

PATHOLOGY OF CONVALESCENT POLIOMYELITIS IN MAN. J. H. PEERS, *Am. J. Path.* **19**:673 (July) 1943.

Peers describes the pathologic aspect of the residual lesions of 3 patients with poliomyelitis who had

survived seven, five and eighteen and one-half weeks from the onset of illness. Lesions in the cerebral cortex, consisting of perivascular collars of lymphoid cells and interstitial foci of microglia and astrocytes, were confined to the paracentral lobules. Only minimal lesions were observed in the basal ganglia and thalamus. In the midbrain the substantia nigra presented the most severe damage. Lesions in the pons were confined to the tegmentum. Loss of nerve cells was extensive in Deiters' nuclei and more patchy and asymmetric in the motor fifth and seventh nuclei. Single necrotic cells were still present four months after the acute illness. Perivascular infiltration diminished, and the density of fibrous gliosis increased with the duration of convalescence. In the cerebellum, lesions were encountered only in the tectal nuclei and in the cortex of the vermis. The most prominent changes in the medulla consisted of loss of cells and scarring in the reticular substance similar to that present in the pons. The spinal cord presented an almost complete loss of nerve cells throughout the entire length of the anterior gray substance. In contrast, the lateral horns were comparatively spared; lesions in Clarke's column were patchy and asymmetric, and no definite changes appeared in the posterior horns. Replacement gliosis in the anterior horns was at first abundant but delicate, with bulky astrocytes. Later the cells shrank, and the fibrils became coarser. In the white matter of the spinal cord there was mild diffuse demyelination of most of the ventral and lateral columns with the exception of the pyramidal tracts. In the posterior columns demyelination was partial and was confined to the region of the comma tracts of Schultze. The anterior nerve roots showed severe degeneration consequent to the extensive loss of anterior horn cells. Almost all the coarse motor fibers had disappeared. In contrast, the fine myelinated efferent sympathetic fibers were mostly spared. In the gasserian, dorsal root and sympathetic ganglia there were a few small foci of lymphoid cells. In the root ganglia only rare cells had disappeared, leaving behind capsules filled with mononuclear cells. The meninges contained only a few scanty foci of lymphoid cells, and no lesions were seen in the choroid plexus.

J. A. M. A.

CHANGES IN THYMUS WITH SPECIAL REFERENCE TO MYASTHENIA GRAVIS. F. HOMBURGER, *Arch. Path.* **36**:371 (Oct.) 1943.

Homburger reports that among 6,000 autopsies performed at the New Haven Hospital 41 instances of tumor or of enlargement of the thymus were encountered. In 27 of these the patients were children under 16 years of age. The remaining 14 cases include 3 of cancer, 3 of enlargement of the gland associated with thyrotoxicosis, 6 of enlargement of the gland encountered incidentally at necropsy and 2 of noncancerous thymic tumor coincident with myasthenia gravis. Epithelial metaplasia was a prominent feature and was accompanied by scarcity of the corpuscles of Hassall in the 2 thymic tumors associated with myasthenia gravis. This observation is in accordance with the conclusions of Bell, Lievre and Norris that thymic tumors in patients with myasthenia gravis are of a distinct type characterized by epithelial metaplasia; it is in contradiction to the more recent opinion stated by Obiditsch and Sloan, who stressed the predominance of lymphoid tissue in thymic tumors of patients with myasthenia gravis.

J. A. M. A.

INTRACRANIAL
NIEMER,
(Oct.) 19

Vonderahe
unsuspected
This tumor
but invasion
and quadri
dorsal surfa
frequent site

Three of
between the
bodies. One
trated the in
right inferio
medullary v
glomatus i
bipolar neur

Vonderahe
develop som
pose tissue;
tion, posses
derivatives,
or during g
as mesoder
from simple
and terator

KERNICTER

FETALIS

McCORN

379 (O

Foster a
2 patients
severe jau
livery, foll
five days
the three
viable fem
The other
parents, p
day and c
received a
month of
Necropsy
Foster a
severe ict
evident.
logic stud

THE CEN

BAKER

Neuro

Baker a
man in v
abdomen,
plegia, re
ness. Sp
Facial dip
the left.
finally es
phyrinuri
normal c
voiding r
photosens
during th
but abou
acute ex

INTRACRANIAL LIPOMA. A. R. VONDERAHE and W. T. NIEMER, J. Neuropath. & Exper. Neurol. **3**:344 (Oct.) 1944.

Vonderahe and Niemer report 4 cases in which an unsuspected intracranial lipoma was found at autopsy. This tumor is usually small and well circumscribed, but invasion occurs in some instances. The tuberal and quadrigeminal regions, the infundibulum and the dorsal surface of the corpus callosum are the most frequent sites of this neoplasm.

Three of the tumors described here were found between the infundibulotuberal region and the mamillary bodies. One of them possessed a pedicle which penetrated the infundibulum. A fourth tumor invaded the right inferior quadrigeminal body and the anterior medullary velum. Two of the tumors were hemangiomas in type, and one contained a collection of bipolar neurons.

Vonderahe and Niemer state that lipomas which develop some time after gastrulation contain only adipose tissue; others, developing shortly after gastrulation, possess more highly differentiated mesodermal derivatives, such as bone; still others, developing before or during gastrulation, possess neuroectodermal as well as mesodermal elements. There is thus a transition from simple lipoma to the more complex teratoid tumor and teratoma.

GUTTMAN, Philadelphia.

KERNICTERUS UNASSOCIATED WITH ERYTHROBLASTOSIS FETALIS. FRANCIS M. FOSTER and RAYMOND A. MCCORMACK, J. Neuropath. & Exper. Neurol. **3**: 379 (Oct.) 1944.

Foster and McCormack report their studies on 2 patients with kernicterus. In 1 Negro male infant severe jaundice developed thirty-six hours after delivery, followed by opisthotonos and rigidity. He died five days after birth. The parents were healthy, and the three preceding pregnancies had resulted in three viable female children. Both parents were Rh positive. The other Negro male infant, a first born of syphilitic parents, presented severe jaundice on the fourteenth day and died on the fifteenth day. The mother had received antisyphilitic therapy, beginning in the sixth month of pregnancy. Both parents were Rh positive. Necropsy was performed in both cases.

Foster and McCormack state that the cause of the severe icterus of the newborn in these 2 cases is not evident. Erythroblastosis fetalis is ruled out by serologic studies, blood smears and autopsy.

GUTTMAN, Philadelphia.

THE CENTRAL NERVOUS SYSTEM IN PORPHYRIA. A. B. BAKER and C. J. WATSON, J. Neuropath. & Exper. Neurol. **4**:68 (Jan.) 1945.

Baker and Watson report the case of a 24 year old man in whom pain developed in the extremities and abdomen, followed within three weeks by flaccid quadriplegia, restlessness, irritability and, at times, impulsiveness. Speech was thick; there was some dysphagia. Facial diplegia was present, and the tongue deviated to the left. A diagnosis of acute idiopathic porphyria was finally established, and laboratory studies revealed porphyrinuria. The diagnosis was delayed because of the normal color of the freshly voided urine. A history of voiding red urine intermittently for one year and of mild photosensitivity with minimal formation of vesicles during the summer was obtained. A remission occurred, but about two and a half years later there was a final acute exacerbation, associated with voiding of reddish

brown urine. The urine gave a strong reaction for porphobilinogen, in addition to zinc uroporphyrin and a fair amount of porphobilin. In a few weeks bulbar involvement occurred, and two months later death ensued.

Necropsy showed no gross abnormalities in the nervous system. Microscopic study revealed evidence of alterations in the neurons and myelin sheaths throughout the brain and the spinal cord, in addition to extensive destruction in the peripheral nerves. The intracranial lesions, though scattered, appeared to be most severe within selected nuclei of the cranial nerves, namely, the nuclei of the facial and hypoglossal nerves and the dorsal nucleus of the vagus nerve.

The role of porphyrins in the production of lesions of the nervous system is not clear. Some studies indicate that, while porphobilinogen itself is innocuous, some pigment derived from it (other than uroporphyrin) may be the substance which is active in producing the nervous manifestations and possibly, also, the abdominal colic.

GUTTMAN, Philadelphia.

A DISTINCTIVE TYPE OF ENCEPHALOMYELITIS OCCURRING AMONG TROOPS IN THE NORTHERN TERRITORY OF AUSTRALIA. JOHN P. HORAN, GEORGE A. W. JOHNSTON, JOHN H. HALLIDAY, J. O'BRIEN and E. WESTON HURST, Brain **67**:93, 1944.

The authors report in detail 2 fatal cases of a previously undescribed type of encephalomyelitis. The first patient had lacerated his left little finger, after which he had a two weeks' illness, thought to have been acute polyarthritis. There developed pain in the left wrist, tenderness of the left ulnar nerve and transient sensory impairment in the distribution of that nerve. Two months after the onset, fever, chilliness, vomiting and headache developed, and the symptoms in the left hand became more severe. At this time he had definite atrophy of muscles supplied by the ulnar nerve. In the course of four days there developed numbness, tingling and weakness of the left leg and nuchal rigidity. The spinal fluid contained 633 cells per cubic millimeter, with a total protein content of 70 to 80 mg. per hundred cubic centimeters. During the ensuing two days he had numbness of the left side of the chest, facial paresis, inability to swallow and dysarthria, and death occurred, as a result of respiratory distress. Pathologic examination revealed that the ulnar nerve was degenerated; both the parenchyma and the sheath had been invaded by leukocytes. The meninges were infiltrated with mononuclear leukocytes. The parenchyma of the central nervous system contained large, sharply demarcated focal necroses, some of which were perivenous. These areas of necrosis contained masses of leukocytes, mixed leukocytes and pleomorphic microglia cells or microglia cells with a few lymphocytes and plasma cells. There was also evidence of diffuse leukocytic infiltration of the parenchyma and microglial proliferation. Alterations of the parenchyma of the central nervous system were most conspicuous in the spinal cord, while the changes in the brain stem and the cerebellum were at an earlier stage. The parenchyma of the cerebrum was not involved. Attempts to culture organisms or a virus were futile.

The second patient had a febrile illness seven days after a tonsillectomy with vomiting and headache, followed after two weeks by diplopia. He had a whitish yellow membrane over the tonsillar region and meningeal signs. The spinal fluid contained 250 lymphocytes per cubic millimeter. Pathologic examination revealed lesions identical histologically with those in the preceding case, occurring in the brain stem and the cerebellum.

The authors conclude that the pathogenic agent entered peripherally in each case and traveled along nerve paths to reach the central nervous system.

FORSTER, Philadelphia.

Psychiatry and Psychopathology

A REVIEW OF CASES OF VETERANS OF WORLD WAR II DISCHARGED WITH NEUROPSYCHIATRIC DIAGNOSES. CHARLES B. HUBER, *Am. J. Psychiat.* **100**:306 (Nov.) 1943.

Huber studied 100 veterans of World War II, all of whom had been discharged for neuropsychiatric reasons. In 99 per cent of cases he felt the precipitating factor could not be considered the stress or strain of actual combat. No outstanding single feature could be found in the family or the personal histories. In some patients, particularly those of the psychoneurotic group, it is possible that the change in environment may have contributed to the onset of the illness. Venereal disease did not play an important role. Huber felt that many of the men could have been rejected prior to induction had proper notation been made of educational advantages.

FORSTER, Philadelphia.

ENURESIS IN THE NAVY. ALEXANDER LEVINE, *Am. J. Psychiat.* **100**:320 (Nov.) 1943.

Levine studied 150 instances of enuresis occurring among naval recruits. He concluded that enuresis was in itself only a symptom and that it was frequently associated with other symptoms indicative of a deep-seated personality disturbance. The affected men were usually immature, maladjusted and emotionally unstable. The siblings and parents of these patients presented numerous psychiatric abnormalities. In a high proportion of the patients there was present a lack of security, allowing for the persistence of infantile traits.

FORSTER, Philadelphia.

A STUDY OF FORTY MALE PSYCHOPATHIC PERSONALITIES BEFORE, DURING AND AFTER HOSPITALIZATION. W. LYNWOOD HEAVER, *Am. J. Psychiat.* **100**:342 (Nov.) 1943.

Heaver studied 40 males with psychopathic personalities. The diagnostic criteria of Cheney were followed. The average duration of illness was six and three-fourths months. One-half the group had forebears with psychopathic traits, and only 2 had well adjusted mothers. In over one-half the group the home environment was featured by environmental stress. In only 12 instances was a deep insight into the problem achieved. Therapy consisted in a well organized regimen, in addition to psychotherapy. On discharge, the condition of 36 of the 40 patients had improved. Follow-up studies on 31 of the 40 patients revealed that 23 had in some measure become acceptable to society and 16 could be considered as recovered.

Heaver concludes that the pathogenesis of psychopathic personality depends on an infantile pattern of conduct perpetuated unintentionally by parents with unconscious immaturity. Under these conditions emotional adequacy does not develop. The plastic mind of the child is conditioned by uncritical maternal devotion, and he fails to identify himself with his father. On the basis of this arises a protest against his own sex, leading to asocial behavior. The prognosis depends not on the duration of symptoms but on the gravity and dimensions of the conflict nucleus and the ability to compromise.

The therapy of the psychopathic personality and of his family remains a challenge to psychiatry.

FORSTER, Philadelphia.

IMMEDIATE AND FOLLOW-UP RESULTS OF ELECTROSHOCK TREATMENT. LAUREN H. SMITH, DONALD W. HASTINGS and JOSEPH HUGHES, *Am. J. Psychiat.* **100**:351 (Nov.) 1943.

Smith, Hastings and Hughes studied the effects of electric shock therapy administered over a two year period to 279 patients. They concluded that this method is effective in the therapy of involutional melancholia and manic-depressive psychosis. Manic patients were found not to maintain their recovery as well as agitated and depressed patients. There is no evidence that electric shock either prevents a future psychotic attack or interferes with spontaneous clinical recovery. Electric shock was found to be ineffectual in treatment of schizophrenia and of doubtful value in treatment of the psychoneuroses. The use of curare-like medication decreased the incidence of traumatic skeletal injuries. While memory changes always occur during the course of therapy, they do not appear to be permanent.

FORSTER, Philadelphia.

FATAL CATATONIA. OTTO BILLIG and W. T. FREEMAN, *Am. J. Psychiat.* **100**:633 (March) 1944.

Billig and Freeman describe 3 cases of fatal catatonia, all occurring in females with schizophrenia. On the basis of their observations, as well as those reported in the literature, the authors conclude that fatal catatonia is a complication of the usual schizophrenic illness and does not constitute a separate form of the disease. It may occur in apparently healthy persons or appear as an exacerbation in the course of any form of schizophrenia. Prior to the onset of fatal catatonia there is a prodromal phase, lasting from two weeks to several months during which the usual schizophrenic pattern is displayed. The actual catatonic phase may be divided into two subphases: (1) a period of increasing perplexity, anxiety, incoherence and restlessness, associated with a blind drive toward annihilation, suicidal tendencies, acrocyanosis and hypertension, and (2) a phase in which motor restlessness becomes more primitive, consciousness becomes clouded, the blood picture changes, the temperature rises, the blood pressure falls, the pulse becomes weak and rapid, the pupils dilate and the reflexes disappear. Cyanosis appears; there are petechial hemorrhages into the tissues, and respiratory or vasomotor collapse occurs. At autopsy only petechial hemorrhages into the skin and erythropoiesis of the bone marrow are found. Billig and Freeman believe that changes in the hormonal-vegetative system may be responsible for the condition.

FORSTER, Philadelphia.

ANOREXIA NERVOSA: METABOLISM AND ITS RELATION TO PSYCHOPATHOLOGIC REACTIONS. S. M. SMALL and A. T. MILHORAT, *Am. J. Psychiat.* **100**:681 (March) 1944.

Small and Milhorat studied 4 cases of anorexia nervosa, investigating the psychopathologic reactions and their relation to the organic changes and the alterations of somatic functions concerned with metabolism. In all 4 cases there was refusal to eat due to aversion or fear of food. The appetite was not impaired. No specific dynamic factors could be elicited, and frank compulsive features were absent. Restless overactivity

was marked
ment of the
and attentio
urinary an
nitrogen an
studied. T
for postula

SCHIZOPHR
BLANK,
Am. J.

Blank, S
old boy wit
an extensiv
was crowd
almost as
was norma
seclusivene
amination
occupied a
sparse. In
laughter
During the
tions, the
and seclus
jargon ma
in the co
faulty toil
incoherent
the time
made at a
drawn, bl

The aut
tionships
symptoms
yielding h

CHEMOTHE
DRUGS
THIAZ
AND I
and G
Dis. 2

Reynol
use of sm
peutic ag
(gonorrh
especially
informati
logic and
ciency de
what effe
efficiency
of subje
24 army
versity
examinat
line. Su
divided
same tes
only) th
been giv
a total
receiving
thiazole
4 Gm.
of sulfad

was marked and was dependent on anxiety. In treatment of the problem the symptoms were disregarded, and attention was directed to the anxiety. Food intake, urinary and fecal output, basal metabolic rate and nitrogen and creatinine excretion in the urine were studied. The authors conclude that there is no basis for postulating a primary metabolic disorder.

FORSTER, Philadelphia.

SCHIZOPHRENIA IN A FOUR YEAR OLD BOY. H. ROBERT BLANK, OLIVE CUSHING SMITH and HILDE BRUCH, *Am. J. Psychiat.* **100**:805 (May) 1944.

Blank, Smith and Bruch report studies on a 4 year old boy with schizophrenia. The family history revealed an extensive psychopathic trend. The home atmosphere was crowded with fears and terrors, and the mother was almost as sick as the patient. The early development was normal, but there was a gradual development of seclusiveness, terrors, apathy and temper tantrums. Examination revealed that the patient was aloof, pre-occupied and self absorbed, while productivity was sparse. In observed play there was more urgency, and laughter became increasingly shrieking and excited. During the course of nine months' study in group situations, the patient was found to be passive, dependent and seclusive; the productions showed echolalia and jargon manifestations, and contact was transitory. Early in the course of therapy some catatonic features and faulty toilet habits were present. On retiring, he babbled incoherently for long periods and had night terrors. At the time of discharge a happy adjustment had been made at a simple level, but the child remained a withdrawn, blocked and passive personality.

The authors evaluate the familial interpersonal relationships in this case and conclude that the child's symptoms might be considered as defensive stratagems yielding him protection from a threatening world.

FORSTER, Philadelphia.

CHEMOTHERAPEUTIC PROPHYLAXIS WITH SULFONAMIDE DRUGS: II. THE EFFECT OF SMALL DOSES OF SULFATHIAZOLE OR SULFADIAZINE ON MENTAL EFFICIENCY AND HAND-EYE COORDINATION. F. W. REYNOLDS and G. W. SHAFFER, *Am. J. Syph., Gonorr. & Ven. Dis.* **27**:563 (Sept.) 1943.

Reynolds and Shaffer point out that the widespread use of small doses of sulfonamide drugs as chemotherapeutic agents for the prevention of venereal infections (gonorrhea, chancroid and lymphogranuloma venereum), especially by the armed forces, makes desirable some information as to the effect of these drugs on the physiologic and psychologic processes on which fighting efficiency depends. A study was undertaken to determine what effects sulfathiazole and sulfadiazine have on mental efficiency and on hand to eye coordination. Two groups of subjects were used for this study: (1) a group of 24 army medical officers and (2) a group of 49 university senior students. In each group, preliminary examinations were made in order to establish a base line. Sulfathiazole or sulfadiazine was administered in divided doses over a twenty-four hour period, and the same tests were repeated six hours and (in group 2 only) thirty hours after the last dose of the drug had been given. Half of the subjects in group 1 received a total of 6 Gm. of sulfathiazole each, the other half receiving inert placebos similar in appearance to sulfathiazole tablets. In group 2 each of 19 subjects received 4 Gm. of sulfathiazole; 20 subjects received 4 Gm. of sulfadiazine, and 10 subjects were given inert placebos.

Comparison of the sulfonamide-treated groups with the controls reveals no statistically valid change in mental efficiency or hand to eye coordination following either drug. A few subjects receiving sulfathiazole appeared to have an idiosyncrasy to the drug, since their performance was notably below that of all others. None of the subjects given sulfadiazine showed such an idiosyncrasy.

J. A. M. A.

"SHOCK" THERAPIES. GEORGE ALEXANDER, *J. Nerv. & Ment. Dis.* **99**:922 (June) 1944.

Alexander points out that in evaluation of the results of shock therapies there has been failure to consider the time factor properly, so that in some instances improvement occurring two or three months after the cessation of treatment has been attributed to the shock therapy. This tendency disregards the natural trend toward spontaneous improvement of many psychiatric conditions. The author suggests that in any case in which there was not sufficient improvement to allow the patient to leave the hospital within thirty days of the termination of his treatment the therapy be considered to have failed.

CHODOFF, Langley Field, Va.

PROBLEMS OF NAVAL PSYCHIATRY. FRANCIS J. BRACELAND and HOWARD P. ROME, *War Med.* **6**:217 (Oct.) 1944.

Braceland and Rome point out that unfitness for the armed services does not mean that the so-called unfit man is a maladjusted person in the civilian sense. In the armed services a man must adjust completely or he is unfit, and it is the psychiatrist who initiates his discharge. This causes him to be classified as a psychiatric casualty and raises the mistaken impression that because hundreds of thousands of such discharges are made this is a nation of misfits. What this really amounts to is that training, specialization and singleness of purpose in education have made the national quality of adjustment a little too brittle. War brings all emotional and characterologic defects into the foreground because of the tension and pressure under which the group labors. These blemishes are serious from a military standpoint, but they are not disabling on the well cared for face of civilian life.

The psychoses which occur early in the recruit's career, or even later in shore installations, do not differ from those seen in civilian life. One of the few new syndromes has been called "three day schizophrenia." It is an acute fulminant state in which the mental content is indistinguishable from schizophrenia but more confusion and more frequent visual and auditory hallucinations are present. It develops in a previously well adjusted personality and subsides completely in three to five days. It arises in response to environmental stress—overexertion, long periods of sleeplessness, loss of weight and intense activity under trying conditions. Rest and sedation bring about miraculous changes in short periods.

An interesting and noteworthy fact in this war is the rapid and high recovery rate of psychotic patients. Acute psychotic casualties during combat are rare among Naval personnel afloat. Symptoms of emotional distress are common but are not per se a cause for hospitalization. The Navy has designated the symptom complex of heightened irritability, symptoms referable to the autonomic nervous system, fatigue and personality changes occurring after severe combat in a previously emotionally sound person as "combat fatigue." This diagnosis in the Navy is used only as a working basis, and no one is ever discharged with this label.

In this war hysteria is not reported as often as in World War I, and there seem to be more instances of gastrointestinal disturbances and fewer of disordered action of the heart.

Emphasis is on group therapy of a short, active nature, using every possible aid, and recovery is judged in terms of effectiveness rather than of insistence on complete insight.

PEARSON, Philadelphia.

ETIOLOGY AND PATHOGENESIS OF NEUROCIRCULATORY ASTHENIA: I. HYPERTHERMIA AS ONE OF THE MANIFESTATIONS OF NEUROCIRCULATORY ASTHENIA. MEYER FRIEDMAN, War Med. 6:221 (Oct.) 1944.

Approximately 36 per cent of a series of patients with a condition diagnosed as neurocirculatory asthenia were found to have an episodic type of fever, accompanied with moderate tachycardia, increased tremor, localized perspiration and coldness of the skin of the extremities.

Despite extensive clinical, laboratory and roentgenographic investigations, no evidence of infection was found in any of the hyperthermic patients. The character of the fever was found to differ in certain respects from that of fever observed in patients with a typical chronic infectious process. The hyperthermic patients also exhibited during their febrile periods significantly different clinical conditions than those usually found in febrile patients suffering from chronic infectious disease.

Epinephrine hydrochloride, amphetamine sulfate, citrated caffeine, typhoid vaccine and psychic stimuli were found capable of inducing elevations of temperature in these patients during normally afebrile periods. No sedative, however, was found which was capable of preventing or reducing their febrile reactions.

The fever, with its accompanying signs, observed in these patients is thought to result from abnormal activity of the hypothalamus. PEARSON, Philadelphia.

Meninges and Blood Vessels

PRIMARY SYPHILIS TREATED BY TWENTY-SIX WEEK COURSE OF MAPHARSEN AND BISMUTH: ACUTE BASILAR MENINGITIS WITH NEURORETINITIS DEVELOPING DURING TREATMENT. GERARD A. DE OREO, Arch. Dermat. & Syph. 49:109 (Feb.) 1944.

De Oreo reports the case of a patient who had weakly seropositive primary syphilis for which he had received combined therapy. In the thirtieth week of treatment, after a total of forty injections of oxophenarsine hydrochloride (2,400 mg.) and twenty-two injections of bismuth subsalicylate, severe occipital headache developed, followed by a state of excitement, in which he was confused, argumentative, irrational and disoriented. Neurologic examination showed paresis of the left and right abducens nerves. Examination of the fundi revealed bilateral papilledema of 3 to 4 D., the optic disks were indistinct and covered with an exudate and flame-shaped hemorrhages. Visual acuity was impaired. The patient also exhibited moderate stiffness of the neck. The remainder of the neurologic examination revealed nothing unusual except for a slight tremor and some hesitation in the performance of the tests of coordination. The Kahn reaction of the blood was negative. Examinations of the cerebrospinal fluid on two successive days revealed cell counts of 441 and 434 cells per cubic millimeter, with 7 per cent polymorphonuclear leukocytes and the remainder lymphocytes. The Pandy reaction was strongly positive, and the colloidal gold curve was 4455431221.

The Wassermann reaction of the spinal fluid was positive with 0.1, 0.25 and 0.5 cc. and anticomplementary with 1 cc. The diagnosis was acute syphilitic basilar meningitis with neuroretinitis.

The patient's symptoms and abnormal signs disappeared after a course of ten treatments and thirteen injections of neoarsphenamine and five injections of bismuth subsalicylate. The cerebrospinal fluid revealed only 7 cells per cubic millimeter, with a trace of globulin and an almost normal colloidal gold curve. The Wassermann reaction of the spinal fluid showed a slight decrease in titer.

The author states: "Perhaps the one warning note was the low titer of the serologic reactions early in the disease and the speed with which it began to decrease, with complete reversal in three months. In the light of the unfortunate relapse, the serologic reactions must be interpreted as a result of poor immunologic response rather than of prompt therapeutic effect. The persistently negative Kahn reaction and the only temporary relapse of the Wassermann reaction in the face of an almost overwhelming meningeal involvement may be further expression of a lack of immunity. Fever cabinet therapy combined with administration of neoarsphenamine has resulted in clinical recovery and satisfactory improvement of the condition of the spinal fluid."

GUTTMAN, Philadelphia.

BINOCULAR PAPILLEDEMA IN A CASE OF TORULOSIS ASSOCIATED WITH HODGKIN'S DISEASE. MARTIN COHEN, Arch. Ophth. 32:477 (Dec.) 1944.

Cohen reports a case in which torulas were demonstrated in the brain tissue, as well as in the secretions covering the cortex of the cerebrum and the pons, with production of leptomeningitis at the base of the brain. Edema of the brain was present, with dilatation of the ventricles. The aqueduct of Sylvius was partially occluded by exudate. These pathologic changes were the result of the torular infection. The unusual feature in the case was pronounced binocular papilledema due to Hodgkin's disease.

SPAETH, Philadelphia.

CONGENITAL ARTERIAL ANEURYSM AT THE PAPILLA. FREDERICK H. THEODORE AND WILLIAM H. BONSER, Arch. Ophth. 32:492 (Dec.) 1944.

The anatomy of the optic papilla is so important that any deviations from the normal must be seriously considered. There is considerable confusion in the classification of aneurysms of the retinal vessels, and it is convenient to divide the lesions in the various cases thus far reported into three types: (1) aneurysms of the larger branches of the central retinal artery, all of which appear to have occurred secondary to vascular disease or trauma, and which are generally associated with visual impairment; (2) miliary aneurysms, which are of two types, one essentially a senile degenerative phenomenon and the other neoplastic, and (3) arteriovenous aneurysms, which are essentially congenital in origin and are often without associated visual disturbances. The third category is of additional interest in that recent articles have called attention to the association of this striking anomaly with similar arteriovenous aneurysms in the skin and brain. The aneurysm in the case reported corresponded to none of these types but resembled the third in several important details, although the aneurysm was entirely arterial.

SPAETH, Philadelphia.

MENINGOCOCCUS
TOLPIN
70:492

Mewborn
demic meni
News, Va.,
prevalence
become a
repeated pu
intervals.
atypical fo
Absence o
exclude me
stiff neck a
are reporte
was little o
coccic pneu
treatment.
children an
The averag
to adequat
to forty-ei
the early p
blood by a
maintenanc
produced l
(a) alkaline
nalysis and
and (c) d
renal lesio

AFTER-IM
TAINING
W. P.
1945.

The ins
positive a
jects them
lines is pr
ing the
minutes,
field, thu
after-imag
The ph
and studi
means of
suppose
patient v
there mig
ing to th
visual sy
Accord
method
The meth
iner. 2.
fixation p
with any
method i
the after
of an ob
for child
Fields ca
with tur
roentgen
sclerosis
any typ
change.
technicia

MENINGOCOCCIC MENINGITIS. E. B. MEWBORNE, I. S. TOLPIN and G. HIRSCHBERG, Virginia M. Monthly 70:492 (Oct.) 1943.

Mewborne and his associates report 27 cases of epidemic meningitis at the Riverside Hospital, Newport News, Va., during a six month period. During increased prevalence of epidemic meningitis spinal puncture should become a routine measure. In all questionable cases repeated punctures should be done at twenty-four hour intervals. It is essential to watch for cases of the atypical form, such as the severe septicemic form. Absence of signs of meningeal irritation does not exclude meningitis. The authors cite 3 cases in which stiff neck and Kernig's sign were absent. Three cases are reported because of the rapidity of onset; there was little or no prodromal period. In 1 case meningococcic pneumonia developed, which did not respond to treatment. Age plays a decisive part in prognosis; in children and young persons the outlook is favorable. The average case of epidemic meningitis will respond to adequate sulfadiazine therapy in from twenty-four to forty-eight hours. Treatment should be aimed at the early procurement of a high sulfadiazine level in the blood by a high initial dose followed by an adequate maintenance dose. Renal complications due to toxicity produced by the drug can be averted or mitigated by (a) alkalization and forcing of fluids, (b) daily urinalysis and charting of the intake and output of fluids and (c) discontinuance of sulfadiazine when signs of renal lesions develop.

J. A. M. A.

Diseases of the Brain

AFTER-IMAGE PERIMETRY: A RAPID METHOD OF OBTAINING VISUAL FIELDS; PRELIMINARY REPORT. W. P. WILLIAMSON, Arch. Ophth. 33:40 (Jan.) 1945.

The instrument which Williamson used utilizes the positive and negative after-images as the patient projects them on a translucent cover, as a design of white lines is projected on a black background. After studying the positive and negative after-images for two minutes, the patient is able to chart his own visual field, thus outlining any areas not visualized in the after-image.

The phenomenon of after-image has long been known and studied, but it has apparently not been used as a means of perimetric determination. It is reasonable to suppose that if an after-image were produced in a patient with a lesion of the central optic pathways there might be a defect in the after-image corresponding to the site and size of the area of damage of the visual system.

According to the author, the advantages of this method of obtaining visual fields are as follows: 1. The method is not tiring to the patient or to the examiner. 2. The patient is unable to look away from the fixation point, since the after-image moves simultaneously with any shift of the eye. 3. With a hand lamp the method is readily adaptable to the bed patient, who sees the after-images on the ceiling. 4. With a simple design of an object in each quadrant, the method can be used for children, who find the phenomenon attractive. 5. Fields can be conveniently determined daily for patients with tumor of the pituitary gland who are receiving roentgen ray therapy, for patients with active multiple sclerosis with changing scotomas or for patients with any type of abnormal visual fields undergoing rapid change. 6. The method is time saving, enabling one technician to increase the number of fields charted

from seven to seventy or more a day. 7. It is readily adapted to the physician's office. 8. It can be used in processing methods, such as routine examinations for the armed services. 9. The apparatus is simple and easily available, since it consists only of a flood lamp and a cloth shield, which any seamstress can prepare overnight.

The disadvantages are as follows: 1. The normal blindspot is not visualized, since it has no cortical representation. An enlarged blindspot, however, can be visualized in the after-image. 2. It will no doubt prove to be less accurate than the tangent screen method, though thus far it appears to be accurate enough for clinical use. This can be determined only after further study. 3. With the present technic the portion of the peripheral field tested does not represent more than 45 degrees. 4. The method reveals only absolute field defects.

SPAETH, Philadelphia.

CYSTIC HYDROPS OF THE PINEAL GLAND. JESSE L. CARR, J. Nerv. & Ment. Dis. 99:552 (May) 1944.

Cysts of the pineal gland are of three types: (1) small single or multiple cavities, which cause no enlargement of the gland and are present in 38 per cent of pineal bodies examined; (2) cysts associated with pineal tumor, particularly teratoma and pinealoma, and (3) cysts not associated with tumor, usually single and large enough to distend the gland and to cause pressure symptoms.

Carr reviews the literature on the last type, which is called hydrops cysticus glandulae pinealis. Of the theories of the origin of pineal cysts, that of glial degeneration due to ischemia is the most widely held. The clinical picture of cystic disease of the pineal gland consists of a combination of neurologic and endocrine signs. Although precocious senility has been reported, macrogenitosomia has not been attributed unequivocally to a non-neoplastic pineal cyst.

The author reports the clinical and autopsy records of 6 cases of cystic hydrops of the pineal gland. In 2 cases the patient suffered from a depressive psychosis, ending in each instance in a sudden decision to commit suicide. This points to a possible relation between mental disease and cystic hydrops of the pineal gland. In 3 cases there was sudden death. The possibility that precocious senility may be associated with degeneration of the pineal parenchyma is illustrated in a case in which extraordinarily sclerotic arteries about the thyroid were noted. In half the cases some degree of internal hydrocephalus due to compression of the iter was present. The contents of the cysts varied from clear fluid to amorphous debris. In none of the cases was a clinical diagnosis of cystic hydrops of the pineal gland made or suspected.

CHODOFF, Langley Field, Va.

BULIMIA ASSOCIATED WITH EPILEPSY IN CHILDREN. B. VIJNOVSKY, Rev. argent. de neurol. y psiquiat. 9:344 (Sept.) 1944.

Vijnovsky reports 18 cases of bulimia among 66 epileptic children. The symptom had been present since birth in 10 cases, appeared simultaneously with the attacks in 4 cases, five years before the onset of attacks in 1 case and nine years after the onset of attacks in another case. In 1 case the bulimia was accompanied by polydipsia; in another an episode of intense hunger was the prodrome of an epileptic attack. In 4 cases the bulimia disappeared simultaneously with the disappearance of the attack. No increase in weight was observed in spite of the excessive intake of food. In 9

cases blood sugar levels were determined, and they were all normal (80 to 110 mg. per hundred cubic centimeters). In 2 cases pica was present. The author believes that the increase in appetite is due to an epileptogenous focus in the frontal lobe which, at the same time, inhibits lower, probably hypothalamic, centers controlling appetite.

SAVITSKY, New York.

ACUTE MULTIPLE SCLEROSIS. ALUIZIO MARQUES, Rev. *neurolog. de Buenos Aires* 8:271 (July-Sept.) 1943.

Since Babinski called attention to the acute form of multiple sclerosis, in 1885, there has been a considerable difference of opinion as to the relation of this form of multiple sclerosis to disseminated encephalomyelitis. The author believes these two conditions are distinct clinically, although histopathologically they cannot be differentiated. The acute form of multiple sclerosis rarely lasts more than a year; muscle atrophy is commoner than in the chronic form; there is more frequent involvement of the brain stem, especially the bulb, and mental changes are more common. McAlpine called attention to the following important differences between multiple sclerosis and acute disseminated encephalomyelitis: 1. The presence of a febrile reaction is in favor of encephalomyelitis. 2. Pain is rarer in multiple sclerosis than in the infectious disease. 3. Euphoria is rare in cases of encephalomyelitis. 4. One seldom encounters depressed reflexes in cases of multiple sclerosis. The author reports 1 case each of acute multiple sclerosis and encephalomyelitis disseminata. Not more than 50 verified cases of acute multiple sclerosis were found in the literature.

In the first case, a woman aged 35 had an illness of five months, ending in death. During convalescence from malaria, she began to complain of weakness in the lower limbs and of diminution of vision in the right eye. She was hospitalized two months after the onset of the disorder. Neurologic examination soon after her admission to the hospital showed scanning speech, horizontal nystagmus, cerebellar signs in all extremities, absence of abdominal reflexes, exaggerated knee and ankle jerks and positive Babinski, Rossolimo and Mendel-Bechterew signs; there was decided diminution of vision with optic nerve atrophy bilaterally. Examination of the spinal fluid revealed nothing abnormal. There was a rather pronounced remission for about three weeks, followed by complete amaurosis, confusion, incontinence, marked cerebellar signs and spasticity in the lower limbs. Soon afterward there was flaccid quadriplegia, with absence of all reflexes, both deep and superficial. Just before her death there was evidence of involvement of the medulla.

Autopsy showed many patches of demyelination and necrosis, especially in the periventricular and subependymal regions. Myelin sheaths and axis-cylinders were destroyed; little glial proliferation had occurred within the zone of necrosis. There was a considerable amount of cellular infiltration, chiefly lymphocytic and perivascular, and numerous compound granular cells were noted. Around the lesions was intense proliferation of protoplasmic astrocytes. The lesions were more accentuated in the posterior part of the lateral ventricles. There were numerous foci of cellular infiltration, especially in the medulla. Similar areas of degeneration were noted in the cervical portions of the posterior columns.

In the second case an 18 year old white Brazilian youth had sudden onset of the disease four days prior to admission, with choking sensations, which were soon

followed by paresthesias in the upper and then in the lower limbs. After a few hours the lower limbs became paralyzed, and soon afterward the upper limbs were involved. Paralysis of the right arm cleared up the next day. The patient was unable to urinate spontaneously. Neurologic examination showed flaccid paraplegia, with absence of superficial and deep reflexes; there were no ocular lesions and no mental changes; the left arm was paralyzed. The patient had to be catheterized. Bed sores appeared and became infected but improved later. The patient continued to be gravely ill for about six months. The case was considered to be one of acute encephalomyelitis.

SAVITSKY, New York.

Diseases of the Spinal Cord

EFFECT OF ACTIVATED SLUDGE PROCESS OF SEWAGE TREATMENT ON POLIOMYELITIS VIRUS. H. J. CARLSON, G. M. RIDENOUR and C. F. MCKHANN, JR., *Am. J. Pub. Health* 33:1083 (Sept.) 1943.

Carlson and his associates investigated the effect of the activated sludge process as used in municipal sewage disposal plants on the removal or inactivation of a mouse-adapted strain of poliomyelitis virus. Virus suspension 1:300 was used in sludge concentrations of 1,100, 2,200 and 3,300 parts per million with aeration periods of zero, six and nine hours. The results indicate that activated sludge in amounts as low as 1,100 parts per million with six hours' aeration will remove or inactivate the virus to a sufficient extent to reduce greatly infectivity for mice given intracerebral injections. Heavier concentrations of sludge with longer aeration periods largely eliminate infectivity.

J. A. M. A.

RECENT ADVANCES IN TREATMENT OF RUPTURED (LUMBAR) INTERVERTEBRAL DISKS. W. E. DANDY, *J. M. A. Alabama* 13:129 (Oct.) 1943.

According to Dandy, spontaneous cures in cases of ruptured intervertebral disk are rare, although temporary remissions are the rule. There are two components of a ruptured disk: (1) the necrotic interior causing backache, and (2) the protruding portion, causing sciatica. The diagnosis of a ruptured disk is made solely from the signs, symptoms and roentgenographic results of examination of the spine. Spinal injections of contrast medium and spinal punctures are contraindicated; they are unnecessary, and they will lead to the diagnosis of only one third of the total number. The small (concealed) disks outnumber the protruding ones 2 to 1. They cannot be detected with spinal injections of contrast mediums. Two disks are involved in about 80 per cent of cases, and occasionally there is a third ruptured disk. The exposure is unilateral and between the laminae without removal of bone (Love's operation), or, when the interlaminar opening is too small, the removal of a small bite of lamina may be necessary. Mobility of the vertebra, tested by pressure on the spinous process, will usually determine whether the disk is the fourth or the fifth lumbar (98 per cent are at these two disks) or both. The entire necrotic content of the interior of the disk should be thoroughly removed with curets. This is the best insurance against recurrences. Fusion operations are unnecessary and are contraindicated. Fusion of the vertebrae occurs after removal of the necrotic contents of the disk. The reason for the localization of 98 per cent of the rup-

tured lumbar a shift in from the h

ATTEMPTS
FRUIT,
STOOLS
TISCHE

Toomey
the virus o
water, sto
chickens f
poliomyelit
have been
could not
cotton rat
as the test

ASPECTS OF
Rev. a
1944.

Lambrus
of tabes d
encountere
athies wer
lumbar po
other a hi
3 cases in
author con
in cases of
ber of cas
ment abou
was a que
joint. He
accounting
joint. In
He attribut

PARALYSIS
CURREN
CARCIN
1944.

Hoarsen
carcinoma
dence of
the breast
nerve on
the chain
laryngeal

V
THE EF
OF W
GROAT
1944.

Weil a
57 days
operation
The ob
and fema
of the br
in other

tured lumbar disks to the fourth and fifth is probably a shift in the plane of the lateral articular processes from the horizontal to a transverse direction.

J. A. M. A.

ATTEMPTS TO RECOVER POLIOMYELITIS VIRUS FROM FRUIT, WELL WATER, CHICKEN CORDS AND DOG STOOLS. J. A. TOOMEY, W. S. TAKACS and L. A. TISCHER, *J. Pediat.* **23**:168 (Aug.) 1943.

Toomey and his associates made attempts to recover the virus of poliomyelitis from fruit (washings), well water, stools from sick dogs and cords of paralyzed chickens found in vicinities where cases of human poliomyelitis had occurred. Although the virus may have been present in the specimens tested, its existence could not be demonstrated when either the eastern cotton rat or the *Macaca mulatta* monkey was used as the test animal.

J. A. M. A.

ASPECTS OF TABES DORSALIS. CARLOS LAMBRUSCHINI, *Rev. argent. de neurol. y psiquiat.* **9**:281 (Sept.) 1944.

Lambruschini reports 22 personally observed cases of tabes dorsalis, with emphasis on neuroarthropathies encountered with this disease. In 2 cases polyarthropathies were present; in 1 a knee, a hip joint and the lumbar portion of the spine were involved, and in the other a hip and the spine were affected. There were 3 cases in which only one joint was involved. The author comments on the absence of optic nerve atrophy in cases of arthropathy, though he admits that his number of cases is insufficient to warrant a definite statement about this correlation. In 1 of the cases there was a question about the etiologic role of trauma to the joint. He does not believe that injury is significant in accounting for the localization of the changes in the joint. In 2 of the cases there was significant anemia. He attributes this anemia to the syphilitic process.

SAVITSKY, New York.

Peripheral and Cranial Nerves

PARALYSIS OF THE LARYNX: AN EARLY SIGN OF RECURRENCE FOLLOWING RADICAL MASTECTOMY FOR CARCINOMA. J. R. FOX, *Arch. Surg.* **49**:388 (Dec.) 1944.

Hoarseness occurring after radical mastectomy for carcinoma of the breast is often the first clinical evidence of metastasis. Metastasis from carcinoma of the breast causes paralysis of the recurrent laryngeal nerve on the same or on the opposite side by involving the chain of lymph nodes surrounding the recurrent laryngeal nerve. Six illustrative cases are reported.

LIST, Ann Arbor, Mich.

Vegetative and Endocrine Systems

THE EFFECT OF ADRENALECTOMY UPON THE BRAIN OF WHITE RATS. ARTHUR WEIL and RICHARD A. GROAT, *J. Neuropath. & Exper. Neurol.* **3**:374 (Oct.) 1944.

Weil and Groat performed adrenalectomies on 2 rats 57 days old and killed them seventy-five days after operation.

The observations indicate that adrenalectomy in male and female rats is followed by an increase in the weight of the brain. This is due to an increase in water and in other compounds, such as neutral fats, fatty acids,

cholesterol and its esters, without any notable change in the qualitative composition of the brain and the proportional distribution of the different compounds. In the male rat the testes and prostate gland are increased in weight. In both sexes the heart and thyroid increase in weight without any change in the hypophysis.

GUTTMAN, Philadelphia.

PEPTIC ULCER IN THE CANADIAN ARMY (1940 TO 1944). W. R. FEASBY, *War Med.* **6**:300 (Nov.) 1944.

Feasby found that only 10 per cent of a selected group of men with healed duodenal ulcer were able to carry on indefinitely after return to duty, either in England or in Canada. In induction examinations there is an error of about 12 per cent in the diagnosis of duodenal ulcer.

PEARSON, Philadelphia.

Treatment, Neurosurgery

STUDIES ON 2-SULFAMIDO-4-METHYL-PYRIMIDINE (SULFAMERAZINE, SULFAMETHYLDIAZINE) IN MAN: III. TREATMENT OF MENINGOCOCCIC MENINGITIS, W. I. GEFTER and others, *Am. J. M. Sc.* **206**:211 (Aug.) 1943.

Sulfamerazine is one of several methyl homologues of sulfadiazine. Gefter and his associates used sulfamerazine for meningococcic meningitis during an epidemic of that disease in Philadelphia in the winter of 1942-1943. They report observations on 45 patients. The initial dose was always given intravenously as sulfamerazine sodium (5 per cent solution in sterile distilled water), adults receiving 3 Gm. and children 1 to 2 Gm. This dose was immediately followed by oral administration of the drug, adults receiving 1 Gm. every four hours and children 0.25 to 1 Gm. every six hours. Delirious or comatose patients were given the drug by nasal tube until they were capable of taking medication by mouth. Sulfamerazine was continued until the patient appeared entirely well clinically. In the successfully treated group the average total dose of the drug for adults was 56.4 Gm., given over an average period of nine and a half days; the children received an average total dose of 19.3 Gm., over an average period of eight and six-tenths days. Five of the patients were given antimeningococcus serum intravenously, in addition to sulfamerazine. Determinations of the amount of free drug in the blood were made at frequent intervals. Three deaths occurred in this series, a mortality of 6.7 per cent. This is to be compared with the 57.5 per cent mortality occurring in 40 cases of this disease at the Philadelphia General Hospital during 1935, 1936 and 1937, and with the 40 per cent of 50 cases reported in 1942. The results also compare favorably with those in which sulfadiazine was employed (12.5 per cent mortality). Clinical improvement, with return of mental clarity, occurred in 70 per cent of the patients within forty-eight hours. The average time observed for the return to normal temperature was five and two-tenths days. Toxic reactions attributable to sulfamerazine, occurring in each instance after the fifth day of treatment, were noted in 11 patients.

J. A. M. A.

CRANIOCEREBRAL WOUNDS: EXTERIORIZATION METHOD OF TREATMENT. J. BROWDER, *Am. J. Surg.* **62**:3 (Oct.) 1943.

Browder for several years has been applying a method for treatment of neglected wounds of the brain

which is patterned after the plan of exteriorization of cerebral abscess as recommended by King. This method prevents the formation of fungus cerebri. The scalp, bone, dura and brain are debrided, and all softened cerebral tissue is removed by suction, hemostasis being secured by applying the electrocoagulating current to the metal tube of the sucker whenever a blood vessel is drawn into it. The dura should be cut away to the limits of the cerebral defect. After débridement, cerebrospinal fluid should be withdrawn through the spinal needle in order to reduce the possibility of cerebral herniation. After the cerebral cavity has been opened widely, the entire area is covered with a single layer handkerchief of mesh gauze (44 by 40 per square inch). Sulfanilamide crystals are blown on to the handkerchief lining the cavity. The cavity is then packed with $\frac{1}{2}$ inch gauze strips to the level of the scalp. The flaps of scalp are brought over the area and loosely approximated. A snug-fitting dressing composed of wet, flat gauze, held firmly in place by a skull cap, should be applied to prevent herniation. The wound is not dressed for three to five days. For dressing the patient is placed on his side, cerebrospinal fluid is withdrawn from the lumbar thecal sac, the wound is reopened and the gauze pack is removed. The cavity lined with the adherent gauze handkerchief is filled with full strength hydrogen peroxide and washed out with saline solution. This should be repeated three or four times before an attempt is made to loosen the handkerchief. The removal of the lining gauze at the first dressing is a slow and tedious procedure, but each dressing becomes less arduous. In about ten to twelve days the entire cavity is covered with granulation tissue, the surface of which must not be injured during dressings. Slowly the cerebral wound becomes smaller, and finally, by gradual decrease in the amount of intracranial packing, the granulating surface rises to the level of the cranial vault. After epithelization becomes complete, plastic repair of the scalp and cranial defect may be carried out.

J. A. M. A.

GENERAL SANARELLI-SHWARTZMAN PHENOMENON WITH FATAL OUTCOME FOLLOWING TYPHOID VACCINE THERAPY. ERICH URBACH, HAROLD L. GOLDBURGH and PHILIP M. GOTTLIEB, *Ann. Int. Med.* **20**:989 (June) 1944.

Urbach, Goldburgh and Gottlieb report the case of a woman aged 40 who was treated for "infectious arthritis" with triple typhoid vaccine. After the third treatment (10,000,000 organisms given by the intramuscular route and 75,000,000 injected intravenously) the patient experienced a severe chill, and within two hours the temperature rose to 99.6 F. and then dropped, precipitously to 96.4 F. The patient went into peripheral vascular collapse and died six and one-half hours after the injection. Necropsy revealed widespread cutaneous and visceral petechial hemorrhages; lack of coagulation of the blood, and intense congestion of the lungs, intestines and muscles, associated with necrosis of the kidneys, liver and adrenal glands. These observations correspond to the changes associated with the general Sanarelli-Shwartzman phenomenon in experimental animals.

GUTTMAN, Philadelphia.

THE TREATMENT OF RHINORRHEA AND OTORRHEA. W. E. DANDY, *Arch. Surg.* **49**:75 (Aug.) 1944.

Cerebrospinal fluid rhinorrhea and otorrhea result from abnormal fistulous openings between the subarachnoid or ventricular spaces and the accessory paranasal

sinuses or mastoid air cells. These conditions are most frequently caused by fracture of the skull or an opening created by operation; they are rarely due to erosion produced by tumor or infection or to a congenital defect.

The escape of cerebrospinal fluid may cease spontaneously, as it does in cases of otorrhea following fracture of the petrous bone. Leakage persisting longer than two weeks must be treated surgically, since sooner or later meningitis or brain abscess will develop. While the operation is practically free from danger, death may follow the closure of the fistula if an intracranial infection has already been present.

The fistula may be closed in the following ways: (1) direct suture of the dural opening; (2) dural closure by free fascial transplant; (3) closure of the bony opening by a flap of dura or other soft tissue; (4) sealing of the bony opening with wax.

Dandy reports 11 clinical cases; 8 of the patients were cured permanently by surgical intervention; 2 died of intracranial infection, and in 1 patient the leakage of spinal fluid persisted because the fistula was not found at operation.

As a rule, the location of the fistula can be determined by the site of the causative fracture or operative defect in the skull; in rare instances, however, it may be impossible to find the opening. In 1 observation a fistula could be demonstrated by injection of methylthionine chloride (methylene blue).

Spontaneous pneumocephalus and pencephaly may develop as a result of a ball valve mechanism but may disappear after closure of the fistula.

A fistula through the frontal sinus caused by a depressed fracture is treated by elevating the depressed fragments of bone, suturing or covering the dural defect with fascia and then replacing the fragments of bone. If no depressed fracture is present, rhinorrhea is best treated by formation of a unilateral frontal bone flap on the side of the leakage. If the fistula is not found, a similar operation may have to be performed on the other side; at any rate, two small osteoplastic flaps are preferable to a single large bilateral exposure.

Cerebrospinal rhinorrhea does not always indicate that the fistula originates from the ethmoid or the frontal sinus; it may develop from an opening in the mastoid which drains through the middle ear and the eustachian tube.

LIST, Ann Arbor, Mich.

DIETHYLSTILBESTROL IN THE MANAGEMENT OF PSYCHOPATHOLOGICAL STATES IN MALES. R. M. FOOTE, *J. Nerv. & Ment. Dis.* **99**:928 (June) 1944.

In the cases selected for this study, it was felt that psychosexual conflicts were present as the result of excessive sexual drives. With the idea that gonadal function was responsible and that its partial suppression would effect dissolution of the conflict, diethylstilbestrol was employed for its secondary effect of inhibiting production of androgen. The diethylstilbestrol was given in daily doses of 1 or 2 mg. One case is reported, that of a 19 year old youth who masturbated four or five times a day and displayed intense sexual preoccupations. With diethylstilbestrol therapy there were notable lessening of the sexual drive and improvement in the general personality and behavior. After thirty-two days without treatment his original state returned, but with resumption of diethylstilbestrol therapy improvement again appeared. Encouraging results have been obtained with the use of this therapy in other cases.

CHODOFF, Langley Field, Va.

ARTIFICIAL
CEDURE.
(Oct.)

Carson
ment of p
eleven year
there was
patients
ment in 70
improvement
gonorrhea
deaths am
definitely

Patients
paralytica
to the pu
paralytica
fever ther
fore and c
complicatio
these con
in a patient
patients di

This se
therapy at
of a sleep
six years
air was u
a week, fo
perature o
of 106 F.
"offers the
author ha
patient is

Carson
well with
therapy is
necessity
is easy to
vidual ba
patients w
artificial
out that t
supervision

He call
reports on
ing that
chances fo

NEUROSUR
ADVANC
CENT V

Cooper
nant grow
cord, a ca
of a rib.
treatment
remarkabl
The case
The 6 year
recovered
treatment
health, an
completely

Emphas
ment for
malignant

ARTIFICIALLY INDUCED FEVER AS A THERAPEUTIC PROCEDURE. W. R. CARSON, *Psychiatric Quart.* **17:604** (Oct.) 1943.

Carson describes the results of artificial fever treatment of patients in mental hospitals over a period of eleven years. Of 122 patients with dementia paralytica, there was some improvement in 67 per cent; of 17 patients with cerebral syphilis there was some improvement in 76 per cent; all 5 patients with tabes showed improvement. Patients with acute, sulfonamide-fast gonorrhea responded fairly well to fever therapy. Two deaths among patients with dementia paralytica were definitely associated with treatment.

Patients with pulmonary tuberculosis and dementia paralytica were treated with fever, without any harm to the pulmonary condition. Patients with dementia paralytica who suffered from convulsions were also given fever therapy, with administration of phenobarbital before and during treatment. This method met with no complications. The author does not regard either of these conditions as contraindications to fever therapy in a patient with dementia paralytica, since most untreated patients die in two years or so.

This series of patients were given artificial fever therapy at first by means of general diathermy or use of a sleeping bag and the inductorium. In the past six years the inductorium plus a cabinet with humidified air was used. Treatment was usually given only once a week, for five hours at a time (three hours at a temperature of over 103.6 F. and two hours at a temperature of 106 F. or over). A minimum total of seventy hours "offers the maximum chance of improvement." But the author has "tried not to stop any treatment while a patient is still improving."

Carson feels that the results compare at least equally well with malarial therapy and that therefore artificial therapy is the method of choice, since it "obviates the necessity of introducing another disease into the body; is easy to control; treatment can be given on an individual basis and prolonged, if necessary; and many patients who could not stand malaria are able to take artificial fever without difficulty." However, he points out that too much emphasis cannot be placed on careful supervision during treatment.

He calls special attention to the unanimity of all reports on treatment of dementia paralytica in emphasizing that the earlier such help is given the better the chances for remission.

McCARTER, Philadelphia.

NEUROSURGERY AND RADIATION FOR RELIEF OF PAIN IN ADVANCED CANCER. GEORGE COOPER JR. and VINCENT W. ARCHER, *Radiology* **42:142** (Aug.) 1944.

Cooper and Archer report 3 cases of advanced malignant growths: an angioendothelioma of the spermatic cord, a carcinoma of the breast and a Ewing sarcoma of a rib. Through persistent and repeated roentgen ray treatment of the metastases, each patient enjoyed a remarkable period of survival, in fairly good health. The case of the Ewing sarcoma was most remarkable. The 6 year old victim, with many pulmonary metastases, recovered from a moribund state after roentgen ray treatment. Thirteen years later she was in perfect health, and the roentgenogram of the chest showed a completely normal condition.

Emphasis is placed on the early roentgen ray treatment for localized pain in patients known to have a malignant growth. Even though no metastases are

demonstrable, both the suffering and the chance for pathologic fracture are decreased.

Three other cases of hopeless malignant neoplasm are described, in which neither radiation nor opiates could control the pain. Peripheral nerve injection, posterior root resection and chordotomy respectively produced complete relief from pain for the remaining few months of life.

"When considering the advisability of neurosurgery, the possibility of unpleasant results must be weighed. Loss of sensation, loss of sphincter control, and paralysis are ever present dangers, and the pain should be more difficult to live with than the possible complications before they are risked."

TEPLICK, Washington, D. C.

Diseases of the Brain

MYASTHENIC SYNDROME OCCURRING WITH MALARIA.

MARIO MENDEZ and MANUEL CHAVEZ, *Rev. de neuro-psiquiat.* **7:335** (Sept.) 1944.

Mendez and Chavez stated that they know of no reported case in which a myasthenic syndrome occurred during malaria. They report the case of a boy of 7½ years who sustained a mild head injury toward the end of December 1943. The next day fever developed. He had a few rises in temperature on alternate days, which subsided spontaneously without specific treatment. After the last day of fever, ptosis of the left eyelid appeared and was followed a day later by diplopia. Soon afterward, ptosis appeared on the right side, associated with difficulty in mastication. One week after appearance of the ptosis, the patient had marked dysarthria for twenty-four hours. All the complaints were intensified by fatigue and were more severe toward evening. Later, bilateral ptosis developed, as well as paralysis of the right external rectus muscle, associated with elevations of temperature on alternate days. The patient was admitted to the hospital and soon afterward had two febrile episodes, on succeeding days. Malarial organisms were found in the blood. The fever disappeared on treatment with synthetic medicaments. The bilateral ptosis and paralysis of the right external rectus muscle cleared up temporarily, after a diagnostic injection of prostigmine methylsulfate. During the next few days the myasthenic syndrome cleared up. The Kahn reaction of the blood of the patient and of the parents were negative. The fundi were normal, and the reaction to the Mantoux test was negative.

SAVITSKY, New York.

Encephalography, Ventriculography, Roentgenography

MYELOGRAPHY WITH PANTOPAQUE AND A NEW TECHNIQUE FOR ITS REMOVAL. WENDELL G. SCOTT and LEONARD T. FURLOW, *Radiology* **43:241** (Sept.) 1944.

Scott and Furlow believe that pantopaque (ethyl iodophenylundecylate) is a satisfactory medium for spinal myelography. It is about as opaque and cohesive as iodized poppyseed oil; it has produced no reactions of importance, and its great advantage lies in the fact that it is much more easily removed from the spinal canal than is the iodized oil.

Sedation is induced with morphine before the examination. After spinal tap, 3 cc. of the medium is in-

stilled. The stilet is reinserted, and the needle remains in place during the entire examination. The usual fluoroscopic and spot film technic is employed.

To remove the oil, the patient remains in the prone position and the craniad portion of the column of oil is allowed to flow beneath the tip of the lumbar puncture needle. The stilet is removed, and the spinal fluid is allowed to bubble out without the syringe being attached. By forced expiration against a closed glottis (Valsalva experiment), the intraspinal pressure is increased; the column of oil becomes thinner and rises from 0.5 to 8 cm. in a cephalad direction. In this way the oil, under pressure, comes into intimate connection with the needle tip and flows freely from the needle. The Valsalva maneuver is repeated until all the oil is removed. Twenty minutes is required for complete removal, but occasionally forty minutes is necessary.

The authors were able to remove all but a few drops in 48 of 50 cases. The failures were due to intradural adhesions from a previous laminectomy in 1 case, and to lack of cooperation in the patient, in the other.

The need for myelography in suspected cases of herniation of an intervertebral disk varies with different neurologists and neurosurgeons. The authors believe that if the indications for surgical intervention are so convincing that the surgeon can assume full responsibility for the accuracy of his findings, myelography is not necessary. However, many men prefer support from the myelogram before submitting their patients to a major operation. Myelography is useful for patients with persistence or recurrence of pain after operation. It is also helpful in the positive identification of multiple protruded disks and may spare the patient unnecessary exploration of normal disks.

TEPLICK, Washington, D. C.

Congenital Anomalies

ABORTIVE FRÖHLICH SYNDROME WITH DISEASE OF THE CEREBELLUM AND SPINAL CORD, POLYDACTYLY AND MUSCULAR ATROPHY: A NEW SYNDROME (?). AUSTREGESILLO JR., Arch. brasil. de med. 34:7 (Jan.-Feb.) 1944.

Austregesilo describes a variant of a degenerative disease of which he has not been able to find a case in the literature.

A white laborer aged 32, single, complained of progressive weakness in the lower limbs of seven years' duration. There were pains in the lower limbs of three years' duration, sexual impotence and a history suggestive of mental retardation. The testicles did not descend until the eighth year. The patient had 10 brothers and 8 sisters, all of whom were well. There was no consanguinity. A paternal grandfather had six toes on each foot. A maternal grandfather died at the age of 60, with paralysis of the lower limbs. One cousin had a deformed foot and another bilateral talipes equinovarus.

Examination revealed obesity, feminine distribution of hair, gynecomastia, kyphoscoliosis and bilateral polydactyly (six toes). There were dysidiadokokinesia, ataxia and dysmetria in both upper limbs; atrophy and muscular weakness were present in both lower limbs, especially the left. The flexors were more severely involved than the extensors, especially in the proximal portions. None of the tendon reflexes could be elicited. There was diminished sensation for superficial modalities, especially for temperature, in the lower limbs; these sensory changes were most pronounced in the extra toes; deep sensibility was spared. The superficial reflexes were normal; the Babinski, Rossolimo and Mendel-Bechterew signs were not elicited. Divergent strabismus was noted in the left eye. There was no retinitis pigmentosa; the fundi were normal.

This man had a forme fruste of Fröhlich syndrome, polydactyly, ataxia of the upper limbs and muscular atrophy of the lower limbs.

SAVITSKY, New York.

NEW YORK
AND

BYRON ST

SYMPOSI

President
eral M

Managem
Injuri

The ma
juries rec
life do m
underlying
the bone,
cleansed,
layer, wi
ments of
should be
producing
ments of
within th
sideration

In Sep
an organ
casualties
at the s
surgical
too, wou
medical
on that
surgeons
compound
general l
geons w
accessible
land and
as cente
It was p
would b
rologic
apparatu
of neuro
ated and
be adm

Defini
cranioc
short w
at the p
establis
Even if
clude th
reconstr
the scal
of the p
that cra

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

BYRON STOOKEY, M.D., *President, New York Neuro-
logical Society, Presiding*

Joint Meeting, Nov. 14, 1944

SYMPOSIUM ON INJURIES OF THE NERVOUS SYSTEM

Presidential Address: Surgical Aspects of Peripheral Nerve Injuries. DR. BYRON STOOKEY.

Management and Treatment of Craniocerebral Injuries. DR. LOYAL DAVIS, Chicago (by invitation).

The management and treatment of craniocerebral injuries received in battle and those received in civilian life do not differ in principle. That injury to the underlying brain is far more important than injury to the bone, that a laceration of the scalp should be cleansed, debrided and sutured accurately, layer by layer, with fine suture material, that indriven fragments of bone and metal or other foreign substances should be removed if they can be reached easily without producing further destruction of brain tissue; that fragments of shell should not be probed for if they lie deep within the brain—all of these are accepted basic considerations.

In September 1942 it became necessary to establish an organization for the treatment of craniocerebral casualties in the European Theater of Operations and at the same time to formulate general principles of surgical treatment which would not be too rigid and, too, would guide the younger and less experienced medical officers situated far forward. It was insisted on that early definitive care by experienced neurosurgeons was necessary for the successful treatment of compound craniocerebral injuries. Therefore, certain general hospitals in which well trained neurologic surgeons were stationed, so located that they were easily accessible to the lines of evacuation, both within England and from the Continent to England, were chosen as centers to which these casualties could be taken. It was predicated that unavoidable delay in evacuation would be compensated for by having an expert neurologic surgeon completely equipped with a suction apparatus, electrosurgical unit and other modern pieces of neurosurgical armamentarium, in a hospital so situated and equipped that final definitive treatment could be administered.

Definitive, or reparative, surgical procedures on craniocerebral injuries are designed to prevent or cut short wound infection either before it is established or at the period of inception and to restore function. Once established, infection is destructive of tissue and of life. Even if combated successfully, it may permanently preclude the restoration of function by the most skilful reconstructive efforts. Therefore the decision to close the scalp wound must always be based on an appraisal of the gross appearance and on recognition of the fact that craniocerebral wounds left open are easy prey to

infection. This decision, it was argued, should be made by an experienced and recognized neurologic surgeon.

Further, it was established that neurosurgical teams should be assigned to evacuation hospitals, more closely situated behind the advance of an army, and be composed of younger surgeons well trained in the principles of surgery, and preferably with several months' experience on a neurosurgical service. It was believed that these men could be taught the essentials of the immediate treatment of a compound craniocerebral injury—that is, not to do too much, and not to do too little. In effect, they should cleanse the wound surgically, with emphasis on shaving the hair about the wound, washing the wound thoroughly with soap and water, removing superficial indriven fragments of bone, metal or debris, introducing sulfanilamide or sulfadiazine powder into the depths of the wound, placing a sterile dressing over the wound, securing it in place with a crinoline or light plaster cast and providing the patient with sulfadiazine tablets to be taken during his transportation. In addition, it was believed that such young men would realize the importance of rapid evacuation for definitive surgical treatment and would, therefore, insist on by-passing several medical installations which had been created by armchair surgeons in the Medical Corps during peacetime. It was also advised that the surgeons of these auxiliary or itinerant teams could be sent farther forward to stimulate battalion and regimental surgeons to do likewise and, if possible, to by-pass the evacuation hospital.

As a corollary to this line of reasoning, it was believed that such younger surgeons, devoid of ambition to become neurosurgeons later in civilian life, would not be tempted to do extensive, ill advised surgical procedures far forward, under poor environmental conditions, without adequate equipment and help.

It was emphasized that there are three essential approaches to the application of chemotherapeutic agents to war or to civilian craniocerebral injuries. First, the sulfonamide compounds and penicillin are not substitutes for the surgical excision of devitalized tissue; second, the sulfonamide drugs will permit delay in operation on the wound and minimize the chances of development of infection following careful surgical treatment of the wound, and, third, they will extend the scope of surgical treatment and make it possible to achieve a perfection in results previously considered impossible. From the results of experiments which were then under way in my surgical laboratory on the use of the sulfonamide compounds with gunshot injuries involving peripheral nerves, it was evident that unavoidable delays between injury and definitive surgical treatment could be bridged rather successfully by the judicious use of these agents. Particular attention was called to the use of a sulfonamide jelly, which could be introduced into the depths of a wound immediately after its receipt by the first medical officer who saw the patient, more effectively than the powdered drug could be dusted into the wound. These substances, then, were not considered as substitutes for surgical measures, but chemotherapy did open new and startling possibilities in management of craniocerebral injuries.

From Sept. 1, 1942 until May 1, 1943, 153 men with craniocerebral injuries were evacuated as soon after

injury as possible to four hospitals in England. In two of these hospitals a well trained and recognized neurologic surgeon was in charge, and in the other two were men who had completed a resident general surgical training, which had included a period of service in neurologic surgery. The compound craniocerebral injuries resulted from accidents which occurred while driving jeeps during the black-out and from fragmenting German Oerlikon 20 mm. shells which exploded within our bombers. The closed type of craniocerebral injuries was received in the manner common in civilian life, as well as in bicycling accidents during black-outs.

Ninety-nine men with acute craniocerebral injuries of the closed type, with or without demonstrable roentgenographic evidence of fracture, were treated conservatively and were got up and out of bed at the earliest moment and stimulated to perform light duties about their wards. Of these, 88.8 per cent were returned to their full duty; 5 per cent were returned to the Zone of the Interior; 2.2 per cent were still in hospitals for rehabilitation and, at the time of this study, 4.4 per cent were still in hospital under treatment.

Seven men had acute craniocerebral injuries of the open type which were of noncombat origin, with the dura mater torn, with the cortex exposed and injured or with subdural or subcortical hematomas. One was returned to full duty and 3 to limited duty in the theater of war. Two were returned to limited duty in the Zone of the Interior, and 1 had been sent to a rehabilitation hospital in the theater. Nine men had open craniocerebral injuries received in air combat, and all had metallic fragments driven far into the brain. One returned to duty in the theater, and 8 were sent back to the Zone of the Interior. Thirty-three patients complained of symptoms of the post-traumatic syndrome, and their injuries were classified as of chronic craniocerebral type. The majority of these men were treated primarily in other hospitals before they came under the care of one of these four qualified men, who recognized the importance of getting the patient out of bed as early as possible and of minimizing the nature of the injury to the head for prevention of the post-traumatic syndrome. However, 50 per cent of these patients were returned to duty in the theater of war; 15 were returned to the Zone of the Interior, and 1 was in a rehabilitation hospital. Six patients with old craniocerebral injuries incurred before they had entered the Army, all with damaged cerebral tissue or with osteomyelitis of the skull, were among this group. Three were returned to duty in the theater, and 3 were sent back to the Zone of the Interior, which none of them should have left.

It was not difficult to reduce the frequency of the noncombat compound craniocerebral injuries. Jeeps were driven during the black-out on wholly unauthorized missions, and the average American soldier was not accustomed to bicycling on a twisting, narrow English road during a black-out. The matter of the open head injuries sustained in air force combat was quite different.

That something might be done to prevent these injuries in whole or in part was emphasized by the fate of a Flying Fortress pilot. The co-pilot was more apprehensive of the exploding and multifragmenting, high velocity German Oerlikon 20 mm. shells than was the pilot. He therefore pulled down over his regulation flying helmet the outside, or metal, portion of the regulation issue steel helmet. Without its interliner, this part of the helmet weighs 2 pounds (907 Gm.), and this, together with the fact that it restricted backward

movements of his head and cut off a considerable portion of his temporal fields of vision, made it impractical for the pilot to wear. An Oerlikon shell penetrated the nose of the plane; the initial velocity was reduced, but its fragments, varying in weight from 1 mg. to 20 Gm., with the effective fragments weighing between 10 and 50 mg., numbering thousands and traveling at a velocity of about 500 meters per second, exploded between the pilot and the co-pilot. The right side of the pilot's skull was penetrated by many small fragments, which left no visible evidence of laceration of the scalp or of fracture of the bone. He became unconscious immediately, and his co-pilot, sitting by his side in the field of the burst, but with his helmet protection, brought the plane in. The pilot had left hemiplegia and left homonymous hemianopsia; the co-pilot had three minute holes in the helmet.

As a result of work with this type of injuries in airmen, it was evident that, besides furnishing adequate protection, a helmet should be designed to fit the head closely and should be comfortable, light and of such construction and appearance as to be a desirable piece of protective clothing for the airman. An acrylic resin product which could be molded in segments to fit the skull; which could be placed within a leather flying helmet; which afforded one-third more protection per unit of weight than does 1 mm. of manganese steel, when tested with an electrically fired 50 mg. steel ball; which was an excellent nonconductor of heat and cold; which had a Brinell hardness greater than gold; which fragmented when struck at right angles to the force; which had an impact resistance of 0.1 to 0.3 foot pound, a tensile strength of 9 to 12,000 pounds (41. to 5,450 Kg.) per square inch (6.45 sq. cm.) and a flexural strength of 12,000 to 14,000 pounds (5,450 to 6,350 Kg.) per square inch; which would absorb less than 0.5 per cent of water by weight after immersion for seven days; which would not burn with a flash; which had no tissue reaction, and which would reduce ambient noises around ear phones, such a product would produce a finished helmet weighing 1 pound 8 ounces (680 Gm.). This helmet was presented for consideration and adoption through channels some time ago; but in the meantime airmen continue to be unprotected because they refuse to wear the heavy steel helmet during combat in the air.

Evidence from other sources shed light on the management and treatment of craniocerebral injuries and aided materially in strengthening the policies and organization which had been laid down but which had not undergone the test of combat conditions. For example, the Canadians working at Neurological Hospital 1, at Basingstoke, England, received for treatment 14 men with penetrating craniocerebral wounds after the Dieppe catastrophe. Of these patients, 12 received definitive neurosurgical care within forty-eight hours after injury, 1 after three days and 1 after five days. Only in the last patient did infection of the wound develop. Three of these 14 patients died of general circulatory collapse, and 2 had a permanent residual hemiplegia. Sulfonamide powder was introduced into all of the wounds at the time of definitive treatment.

Of 128 patients with gunshot wounds of the head admitted to St. Hugh's Hospital for Head Injuries at Oxford, England, in a nine month period, 49 were invalided out of the service. Cairns stressed that infection of craniocerebral wounds does not usually occur from the bullet or the shell fragment but comes from the patient's skin or the surgical attendants. A report from Germany in January 1943 indicated that early in the war, when the Germans had complete domination

of the air operating u was the re hands of a discontinued days betw maximum assumed, is without time of the

Even mo rapid evacu to a neuro favorable aids to ca from Maj recital of Africa. A representin Of these p died, a mo patients, 1 validated ou His exper operations forty-eight least as g in more f within eigh results of after injur he said: forward a fully equ seventy-tw there is a a head w vided that tion and p which he obtain by the front possible to to a gene situated.

In additi of seeing Army Me to manag The essen excellent logic surr the evacu Army, c definitive problem o surmount and x-ray injured m

There Russian three larg as we wo hospitals (schools) with the problems treatment by exper by such necessity

of the air over the Continent, they flew a neurosurgical operating unit from one combat area to another. This was the reverse of getting the patient quickly into the hands of a neurosurgeon. This practice has since been discontinued. Tönnies and Sanger believe that four days between injury and definitive treatment is the maximum interval for a successful outcome, and it is assumed, since they did not definitely so state, that this is without the use of the sulfonamide drugs at the time of the injury.

Even more conclusive evidence of the success of rapid evacuation of patients with craniocerebral wounds to a neurosurgeon, properly equipped, situated in as favorable an environment as possible and with sufficient aids to carry out good postoperative treatment, came from Major Peter Ascroft. All will remember his recital of experiences with the British armies in North Africa. Ascroft reported on 516 patients, the series representing two years' experience in the Middle East. Of these patients, 292 had laceration of the dura and 44 died, a mortality of 15 per cent. Of the remaining 226 patients, 124 were returned to duty, and 93 were invalidated out of the service because of the head wound. His experience showed that the results of primary operations in a general hospital carried out as late as forty-eight or seventy-two hours after injury are at least as good as the results of operations performed in more forward areas, where conditions are difficult, within eight hours after injury and are better than the results of operations done from nine to sixteen hours after injury. Ascroft stated the problem clearly when he said: "We believe it is better not to operate in forward areas, provided that the patient can reach a fully equipped base hospital within forty-eight to seventy-two hours of injury. That is not to say that there is any merit in delay for its own sake; the sooner a head wound is operated on the better, always provided that facilities are available for a complete operation and proper after-care." In other words, the results which he, an experienced neurologic surgeon, could obtain by taking his mobile and well equipped unit to the front were much less favorable than when it became possible to evacuate and transport the patient rapidly to a general hospital where he and his teams were situated.

In addition to these experiences, I had the opportunity of seeing at first hand the organization of the Red Army Medical Corps and the methods which it used to manage and surgically treat craniocerebral injuries. The essential principle on which it based its reported excellent results was the utilization of competent neurologic surgeons in hospitals placed as far forward as the evacuation hospital is situated in the United States Army, completely equipped and staffed to perform definitive neurosurgical operations. There was no problem of fixed tables of organization and supply to surmount before electrosurgical units, suction apparatus and x-ray equipment could be placed as close to the injured man as the tide of battle would permit.

There were 16 neurologic surgeons on the various Russian fronts, with 3,200 beds at their disposal, and three large hospitals in the rear, or Zone of the Interior, as we would designate it, with 3,700 beds. The latter hospitals were closely affiliated with medical institutes (schools) where civilian physicians cooperated closely with the army in making studies of the multitudinous problems which concern the future progress of the treatment of neurosurgical injuries. Procedures learned by experience were passed on to the younger surgeons by such close correlation of effort as to obviate the necessity for the young surgeon to concern himself

with discovering already proved methods of technic, to the exclusion of recording observations on clinical material which may never again be equaled for study.

There were other interesting features of the Russian organization for the care of craniocerebral injuries, such as segregation of patients to separate wards, even as far forward as a mobile field hospital, and the insistence on complete records, which accompanied the patient from the time he was first examined by a medical officer until he arrived in a hospital in the rear. Even more striking was the flexibility of organization which permitted a young neurologic surgeon, like Graschenko, to go forward and treat casualties in an advanced area, while the other half of his team remained in Moscow and cared for patients who had been treated and evacuated by them while they served at the front and Graschenko was in the rear hospital. This line of evacuation and continuity along one agreed-on policy of treatment, together with careful records, will make it possible to report studies of craniocerebral injuries received in battle which we in this country cannot duplicate.

This direct and immediate control of the surgeon general of the Red Army over all the activities and responsibilities of the medical corps, without interference from the echelon above, made it possible for Graschenko, for example, to study the course and influence of infection on the healing of craniocerebral wounds and the clinical and bacteriologic results of the application of the sulfonamide compounds to craniocerebral injuries, with an auxiliary microbiologic laboratory staff which accompanied his surgical unit to the front.

Under field conditions, Graschenko studied 100 cases of craniocerebral injuries bacteriologically. In 20.3 per cent of the cases pathogenic organisms were found. In 12.4 per cent sporogenic (putrefactive anaerobes) were present; in 24 per cent aerobic organisms were cultured; in 26.8 per cent coccic infections were present, and in 16.5 per cent miscellaneous organisms were found. Cultures were made from forty-eight to seventy-two hours after injury in a total of 720 cases, and in only 2 cases were the cultures sterile. However, the largest number of the wounds healed primarily without supuration.

After three to four weeks Graschenko found that the wounds showed a flora of pathogenic anaerobes in 12 per cent of cases, aerobes in 20 per cent, cocci in 70 per cent and putrefactive anaerobes in 8 to 10 per cent. Of the 20.3 per cent of patients in whom pathogenic anaerobes were found, 1.4 per cent died in from six to seven days of severe gas bacillus infection. Subacute anaerobic infections of the brain were found in cases of large cerebral fungi, and of 12 patients with such infection, 9 died. Of 32 patients with chronic anaerobic infection of the brain, 10 died. The course of their illness was long, from three to four months, and often encapsulated abscesses were formed, which might open onto the surface or into the ventricles, with the production of severe meningitis. Of 34 patients with mild anaerobic infection of the brain, none died. Graschenko uses a polyvalent serum in prevention of gas bacillus infection of craniocerebral wounds which contain *Clostridium histolyticum*, *Clostridium perfringens*, *Clostridium oedematiens* or *Clostridium oedematis maligni*.

These, then, briefly were the factors, together with experience in civilian practice, which led to a statement of the following creed of principles concerning the management and treatment of craniocerebral injuries, a creed which applies alike to civilian and to battle casualties.

The scalp is richly supplied with blood vessels and offers considerable resistance to infection. The intact dura mater is a good barrier against the spread of infection, and on the whole the meninges have the power of localizing infection. Provided the products of injury and infection are not allowed to gather under pressure, brain tissue resists infection fairly well.

The gentlest surgical procedure in the most skilled hands is damaging to some degree, and damage to the brain is irreparable. Surgical procedures cannot be carried out within the skull effectively without an electrosurgical unit, suction apparatus, proper x-ray equipment, adequate and proper instruments, facilities for the skilful administration of various types of anesthetics and good nursing teams.

Assessment of the condition of a patient with a craniocerebral wound should include consideration of the depth of coma, the presence or absence of shock, the exact nature of the head wound and, particularly, the presence or absence of other injuries. Shock is seldom severe with head wounds, and when present it is usually due to a loss of blood which can be made up quickly. In the case of compound craniocerebral wounds, roentgenograms of the skull are of great value, particularly in the absence of good clinical notes, and often of any kind of record, in judging the depth and nature of indriven fragments of bone and metal and the condition of the dura mater and brain.

Incomplete operations are more dangerous to the patient than the few hours of delay necessary to evacuate the patient to a competent neurosurgeon in a properly equipped environment. There are only three reasons for retaining a patient and performing an operation under adverse conditions: (1) severe shock—after he has been treated for shock the patient should be evacuated as quickly as possible for a definitive operation; (2) intracranial bleeding and compression of the brain, or other bodily injuries requiring emergency surgical intervention, and (3) lack of opportunity to get the patient to a properly equipped center or hospital within forty-eight to seventy-two hours after injury.

The urgency for operation on craniocerebral wounds depends on whether or not the dura mater is penetrated and on the degree of damage to the brain and the number and character of the indriven fragments. There should always be a detailed examination of the central nervous system, with a record of the state of consciousness in terms of the presence or loss of important reflexes and the response to pain, noise or other stimuli. There must always be an examination for other injuries. Wounds of the face, particularly of the orbit, often involve the skull and brain, and the ear drums may be ruptured, with bleeding, by blast, in contrast to civilian injuries. Badly mangled extremities may lead to an inconspicuous head wound being overlooked, just as a serious head wound may lead attention away from wounds of other organs.

Local anesthesia cannot be used as often as one might think possible, and, though sodium pentothal proved very efficient, it is absolutely necessary that good breathing be established before draping of the head and face is completed. Careful shaving and cleansing of the wound and the field of operation are absolutely essential, and the application of colored antiseptic does not take the place of meticulous cleansing of the wound with soap and water. Haste and skimping in the preliminaries do not save time, and carelessness in preparation makes for bad operations.

Scalp incisions vary with each type of wound, but certain general points apply. The edges of the scalp wound should be excised as narrowly as possible, and incisions should extend the wound, if necessary, to give access to the underlying lesion. Missiles destroy the scalp more than ordinary injuries in civilian life, and often the edges of the wound and the bone are burned by high velocity metal fragments. There may be a small superficial wound in the scalp and underlying extensive destruction of the deeper layers. Fractures of the bone may be of all sizes and shapes, and all detached fragments of bone must be removed to discourage the infection and to expose tears in the dura mater or damage to the brain. However, removal of bone must be conservative, and excision of bone *en bloc* should not be done. Local bone decompression is unnecessary.

The dura mater should never be opened if it is intact unless there is an immediate threat to life from a subdural blood clot. If torn, the edges of the dura should be trimmed, but, if possible, removal of large portions should be avoided. The dura may be dissected away from the inner table of the bone, for foreign material may be hidden between the dura and the bone. Indriven fragments of bone have been proved to be present in the majority of cases of abscess following injury to the brain. This is not true of metallic fragments, which usually penetrate deeper than fragments of bone but are probably partially or totally sterilized by their own heat. It should therefore be the object to remove easily approachable fragments of bone and metal, hopelessly damaged superficial brain tissue, blood clots and foreign matter, by gentle suction if necessary. Often the removal of a surface plug of foreign material of this kind will allow more deeply placed debris to well up and out of the wound in the brain. Probing and searching for deeply placed metallic fragments should never be carried out. Good hemostasis, which can be obtained with silver clips; electrosurgery, and use of fibrin foam are essential to good results.

The introduction of sulfanilamide or sulfadiazine powder into the tract and on the surface of the cerebral wound should be a part of the surgical treatment. From a study of experimental gunshot wounds of peripheral nerves and from observations on wounds received in the North African campaign, I believe that the introduction of a sulfonamide jelly into the depths of the wound immediately on its receipt will make it possible to carry out definitive surgical treatment more satisfactorily and with far less danger of the development of a suppurative wound. There is evidence that use of sulfathiazole in wounds of the brain does not have the danger that earlier experimental and clinical reports indicated.

The practice of young, inexperienced surgeons who have been dealing with craniocerebral wounds in certain theaters of war, without the opportunity of guidance and consultation with an experienced neurologic surgeon, of using fascial grafts from cadavers and other diabolically ingenious methods of closing dural tears in freshly received and potentially infected wounds is a comment on poor organization. If the scalp wound can be approximated without tension, it should be closed without drainage. After a drain is necessary when it becomes impossible to close the scalp wound because of a large loss of tissue, but it must be remembered that continued exposure of the brain in an open wound is always followed by infection. Deliberately to pack open a craniocerebral wound with petrolatum gauze, as has been done in mistaken adherence to a general

directive ab
gical judgm
theft of cad
tion, as we
tainly, plas
no place in

Finally, i
and enthus
turn the sk
for the ski
prevent the
distended b
carefully, a
tained tow
returned qu
final rehab
accomplish

Psychiatric System Medical

The pro
system hav
progress of
and treatm
chiatric sta
respect to
labeled psy
matic neur

Because
tion of the
classification
nection wi
been very
lications
to the ner
to the con
grievances
tion or fat
tural chan

The ac
those con
ranging fr
of mild i
injury. I
ness, aut
difficult to
dissociati
is no exte
of mild i
daze may
combat an
gent beha
cases of r
may be
some inte

In the
not alway
defects of
tion may
perception
occur, an
of these
larly in

In oth
symptom
particular
lesions.

The m
that of

directive about war wounds, without using good surgical judgment in opposition to the directive, is, like the theft of cadaver tissue, a reflection on medical organization, as well as on inferior surgical education. Certainly, plastic repair of the skull by any method has no place in the treatment of acute craniocerebral injuries.

Finally, nursing care must be intensive, intelligent and enthusiastic. Sufficient help must be provided to turn the comatose patient frequently, to care properly for the skin, to see that he gets food and fluid, to prevent the extreme restlessness which is produced by a distended bladder or a wet bed and to control sedation carefully, and, last, the proper attitude must be maintained toward the patient's injury, so that he may be returned quickly to activity around the ward and his final rehabilitation may be successfully and speedily accomplished.

Psychiatric Aspects of Injuries to the Nervous System. LIEUT. COL. WALTER O. KLINGMAN, Medical Corps, Army of the United States.

The problems produced by injuries to the nervous system have become increasingly important with the progress of the war. Interrelating problems of appraisal and treatment from the surgical, neurologic and psychiatric standpoints present themselves, particularly with respect to the large group of disturbances that are labeled psychoneurosis, postconcussion neurosis, traumatic neurosis or compensation neurosis.

Because of the difficulties encountered in differentiation of the traumatic and the post-traumatic reactions, classifications of the psychiatric disturbances in connection with injuries of the nervous system have not been very satisfactory. War injuries introduce complications which differ in some respects from injuries to the nervous system sustained in civilian life, owing to the combination of natural anxiety with war stress, grievances, predisposition and circumstances of exhaustion or fatigue, particularly when there is also a structural change in the nervous system.

The acute mental symptoms of cerebral injury are those concerned with disturbances of consciousness, ranging from states of transient interference, in cases of mild injury, to profound coma, in cases of severe injury. In the return from stupor to normal consciousness, automatism and states of dissociation may be difficult to differentiate from other states of complete dissociation in the combat area, particularly when there is no external evidence of a head injury. In some cases of mild injury, momentary stages of confusion or of daze may be followed by automatism and may, in the combat area, lead to confusion and make for unintelligent behavior and incomprehensible actions. In other cases of mild injury without loss of consciousness there may be delayed collapse, after minutes or hours, or some intermittent confusion, with or without automatism.

In the cases of severe cerebral injury recovery does not always follow, and signs of local damage, specific defects of the nervous system and disturbances of function may result. Alterations in memory, orientation, perception, imagination and emotional attitudes may occur, and unstable behavior patterns may result. Some of these functions may be permanently altered, particularly in elderly and in arteriosclerotic subjects.

In other cases it is difficult to evaluate persisting symptoms when recovery stops short of being complete, particularly in the absence of signs of demonstrable lesions.

The most common residual neurologic syndrome is that of headache, dizziness and emotional instability,

and in many cases the picture suggests that in the syndrome or in the origin of the emotional instability there is an interplay of physical and psychologic factors. At this time it is considered impossible by particular clinical criteria to distinguish between a true psychoneurosis of psychogenic origin and one having organic cause, for any symptom may have either factor as a basis.

Definite improvement in the psychiatric management of cerebral injuries in the immediate post-traumatic state has been recently introduced. Graduated programs of activity are frequently started within twenty-four to seventy-two hours after the patient regains consciousness, with early return to light Army duties in two weeks. This therapy attempts complete divorcement from the idea that the injury is serious and that certain symptoms are to be expected. It eliminates the period of incubation, in which the patient meditates on the suffering and derangement of his life. The Army hospital as a rule is not convenient for frequent visiting by well meaning relatives, friends or claim agents. In the combat area, however, the element of secondary gain may be a potent factor with which to contend. The incorporation of convalescent and rehabilitation programs in many Army hospitals must also be credited with much of the beneficial reversal of results and of methods of management now in vogue. In this early phase of activity there is introduced the psychologic help calculated to strengthen the ego by persuasion, strong suggestion, reidentification and stimulation of the ego ideal.

Despite this, however, physiologic consequences of the trauma in many cases affect the function and structure of the brain to the extent that they offer material for the neurosis or activate a latent or an active neurosis of severe degree.

When this results, the emotional attitudes change; the symptoms assume bizarre qualities, and it is time then to evaluate the signs and symptoms and analyze the psychologic and physical factors in the symptom complex. Each case must be studied and treatment instituted according to its merits. Painsstaking neurologic examination, evaluation of emotional factors, psychologic tests and electroencephalographic and pneumoencephalographic examinations may be necessary. In this, evaluation of the emotional factors and methods of combating them have likewise profited by experience in this war. Narcoanalysis, narcosis therapy and narcosynthesis have been used in civilian practice for many years, but their free use has been necessitated and forced into the foreground by the urgent demands for brief, quick therapy in the armed forces. Application of these technics in the prevention and treatment of neuroses following injuries of the nervous system has added understanding of the conflict between the unconscious sources of anxiety and the ego forces and has aided in the evolution of short term technics derived from psychoanalytic principles. Time is gained by this in that the period necessary to work through resistance is eliminated and uncovered anxieties can be tolerated without lengthy strengthening of the ego. Narcoanalysis, followed by psychotherapy as the patient recovers from the narcosis, results often in dramatic release of the unconscious psychologic tensions, strengthens the ego forces and decreases the severity of the superego pressure. This is particularly true of patients with latent anxieties and resentments dating back to earlier periods of life.

Patients with specific handicaps require special consideration through prolonged rehabilitation programs.

Their worries about cure, livelihood, bodily helplessness and future disturbances of social and economic nature are real and offer a tremendous challenge for life in the future without dependence on family or country.

Another clinical picture presented by injury to the cerebrum is that associated with subdural hematoma or effusion. The psychiatric syndromes encountered may be of two types. The most frequent is that of marked retardation in intellectual activity and personality interrelationships, a flat emotional tone, impaired attention and slow responses. Approach to life situations is superficial. In the other, and less frequent syndrome there is a more classic picture, usually associated with the organic reaction types, with impairment of inhibition or restraint, facetiousness, motor restlessness, a labile and explosive emotional tone, poor judgment, undue productivity and expressions of hostility, distractibility, memory failure, perseveration and circumstantiality. Minimal neurologic signs are the rule, and a pneumoencephalogram may be necessary for a final diagnosis.

In another group are the debatable cases in which the relationship between head injury and mental disease is not so clear but in which the trauma may have served to precipitate the psychosis, such as schizophrenia or manic-depressive psychosis, neurosyphilis or other disorder rather than act as the direct etiologic agent.

In other cases, however, the organic mental syndromes following head injury can be delineated as definite post-traumatic psychopathy. In this group there is absence of any signs of a psychopathic state prior to the injury.

Out of wartime experiences have arisen certain facts for emphasis. Many persons who have a disabling neurosis after head injury suffer from a latent or active neurosis before exposure to military life or from a neurosis incidental to the war experience. Several valuable psychiatric factors have been introduced in the management of injuries of the nervous system by the experience of this war. Prophylactic psychotherapy during the management of the immediate post-traumatic phase has reduced the prospect of persistent disability. Application of short term technics of treatment based on psychoanalytic principles, followed by sound rehabilitation programs, has been most helpful in the treatment of injuries of the nervous system with subsequent neurotic expressions. Diagnostic and prognostic aids from psychologic testing, electroencephalography and air encephalography may be necessary in the full appreciation of structural damage or the psychoneurotic state. Patients with mixed pictures of organic and functional disturbances require management according to the merits of their particular cases, through prolonged psychotherapy, programs of rehabilitation or the protective environment of institutional life.

DISCUSSION ON PAPERS BY DRs. STOOKEY, DAVIS AND KLINGMAN

DR. FOSTER KENNEDY: To discuss adequately these three papers would be to go over the whole of medicine and most of war. From Dr. Stookey's paper, I came to the conclusion that every generation must learn from its own experience; this is true of all men, and not of members of the medical profession alone; it is too bad that it is so, for writing was invented to teach the next generation. I do not think that we physicians go back far enough in our reading. I was much surprised to come across the report of an autopsy on the brain written by my grandfather sometime in 1840 which would have borne excellent comparison with any similar report today. I had to go back to the *Lancet*

of 1830 to get modern advice regarding water balance from a man named Harrison, who had ideas on the treatment of cholera which had to do with water balance. I think that Dr. Stookey believes, too, that if the younger men would do what we older ones do not do—go back farther—they would learn more. It is the modern notion that everything one knows occurred the day before yesterday. It certainly did not, and we physicians would understand better the basis of our knowledge if we went back farther in our reading. It is said, "Every book that is written is out of date in five years, and no medical magazine is worth anything if it is a week old." This is nonsense. Such productions are the work of men earnest, anxious and eager; if we are going to continue our constancy of effort, we shall have to ask our students and our young medical officers to go back to former experience in order to learn about the present. There has never been a better description of certain forms of war wounds (and causalgia is one which is a bugbear today) than that written by Weir Mitchell during the Civil War; I wonder how many present day medical officers have read his description of causalgia. We certainly cannot learn any more about causalgia from modern medicine.

It is good to hear Dr. Stookey speak roundly against the "funnel" idea of nerve union. I think that idea sprang from the general tendency to diagrammatic oversimplification. It seemed better to put the nerve fibers in a "directing" funnel and to say that then they would be all right. I am sure the concept is fundamentally unsound, and I am glad Dr. Stookey has said so. There are many more ways of killing a cat than skinning it. It is possible that many nerve injuries can be dealt with better by plastic surgery rather than by the best of nerve grafting. For instance, many facial paralyses can be better handled by dealing with the muscles involved than by operating on the nerve implicated. This idea might have many applications in treatment of peripheral lesions due to the war. Dr. Stookey spoke wisely against nerve stretching. To subject the most highly developed tissue in the body to a traction which it cannot possibly sustain and expect it to function afterward is to err in thinking. It is not only an error in technic but originally an error in thought.

I was glad to hear Dr. Stookey speak of Huber, who has by no means received the credit due him; he did basic work in this field.

I liked Dr. Stookey's idea about nerve banks. If grafting is necessary, nerve banks will be a necessity, to have vital nerve tissue to place in situ at once.

Dr. Loyal Davis told us of sulfonamide drugs, which, unfortunately, were not available in the last war, with the result that one might see then, as I did, 30 or 40 cases of abscess of the brain in one hospital in one day. That horrible period, apparently, is passing and has almost passed. Dr. Davis did not speak, however, of the habitual use of phenobarbital in cases of compound injury affecting the brain. I think every soldier should be sent from the front area in which he has been wounded with a ticket that he has been given phenobarbital and that he should be given phenobarbital, $\frac{1}{2}$ grain (0.032 Gm.) three times a day, for the next year. This medication should be started at the place where he is wounded. It is important to lower the reflex activity of the brain when it has been grossly injured, as is the case with a wound.

About three years ago, in Washington, D. C., I wrote a memorandum urging that it be made compulsory for every American soldier who rides a jeep, a tank or a motorcycle to wear a crash helmet, and I

led a small know whether or not. It shows very tired of fractured skulls and life and cost of adoption of spirit, can do know that armor of the be used with casualties in warfare. These fragments of the body protect of the medical protection than

I was in Russia—in front line to be produced continuity in so, identity a great advantage it the sick treatment from where he is an advantage to reach it way of flat country lives. However, the and sociology up here.

Colonel interested in consciousness paper read (Tr. Am. enormously concussion. through the remain entire back of his Denny-Brown due to motion the blunt instrument of the missile. S cephalic and to be given taught that the response to have been mesencephalic (though I "governed" One's ability nance of the

Colonel "the future thought of is, in the Every man head than arm or his not know injury to the

led a small campaign in behalf of the idea. I do not know whether it has been made an official order or not. It should be. Certainly, in World War I I got very tired of seeing motorcycle dispatch riders with fractured skulls. It is a lamentable waste of young life and could easily be avoided by the compulsory adoption of crash helmets. Dr. Davis gave you an example of what body armor, put on in no matter what spirit, can do in the preservation of life. I am glad to know that body armor is coming back. Certainly, armor of the middle torso and armor of the head can be used which will reduce by half the number of casualties that might occur in both air and ground warfare. The vast majority of men are not destroyed by great bomb damage; they are defeated by fragments. These fragments, in turn, can be combated by proper body protection. Not enough care is given by the head of the medical corps in any army to the kind of protection than can be afforded the soldier.

I was much interested in Dr. Davis' comment on Russia—in the continuity of medical opinion from the front line to the rear. I do not know how that could be produced in this country unless there can be obtained continuity in education, continuity of experience and, so, identity of opinion. I am sure that in technic it is a great advantage to have that identity of opinion; by it the sick man, the injured man, can be given standard treatment from the place where he is hurt to the place where he is finally going to get well or die. This is an advantage. I am not sure, however, that in order to reach it one would not have to give up more in the way of flattening out the differences by which this country lives than one would gain for the sick man. However, that is a question with philosophic, political and sociologic implications, which is not to be taken up here.

Colonel Klingman's discussion of unconsciousness interested me very much. No one knows what consciousness is, or unconsciousness either. Jefferson's paper read before the American Neurological Society (*Tr. Am. Neurol. A.* 79:13, 1943) was, I thought, enormously illuminating, as is Denny-Brown's work on concussion. Certainly, one knows that a man shot through the frontal lobe with a revolver bullet may remain entirely conscious but that if he is hit on the back of his neck with a sandbag, he goes out instantaneously. Denny-Brown seems to have demonstrated that this is due to movement of the brain in its box induced by the blunt instrument, in contrast to the lack of movement of the brain in the case of the fast-speeding missile. So the government of consciousness is mesencephalic and not cortical. This is something that ought to be given wider recognition. It has been so much taught that the cortex is the highest instrument that the responsibility of the cortex for consciousness seems to have been accepted, whereas the real control is mesencephalic. One may "think" with the cortex (though I do not know that), but one certainly is "governed" by the hypothalamus and the midbrain. One's ability to remain conscious depends on the dominance of the mesencephalon.

Colonel Klingman, I think, wisely pointed out that "the future" will sometime later loom large in the thought of the man who has been hurt in the head, that is, in the place in which he seems to himself to live. Every man is more concerned about an injury to his head than to "some outpost of empire," such as his arm or his leg, or even to some other place he does not know much about, his torso, for example; but an injury to his head produces emotional effects which have

to be considered. The idea of a compensation neurosis is not entirely foreign to the soldier who, having had an injury to the head, looks to the future: Who is going to take care of him? Once I was asked what a civilian compensation neurosis was. I said it was "a state of mind, born out of fear, kept alive by hope of gain, stimulated by lawyers and relatives and cured by a verdict"; and while those words do not apply exactly to some soldiers, they apply to the general idea of the veterans' bonus. I am glad to hear that the medical officers in this war, like Colonel Klingman, are aware of this situation: It has a great deal to do with the future happiness of the soldier and the stability of the country. Colonel Klingman used a phrase which was enormously important—the "inherent adaptive capacity" of man. One may talk as much as one likes about the right technics and about what one will do for this man or that man, but the future of every human being, soldier or civilian, depends on his "inherent adaptive capacity."

DR. JOSEPH E. J. KING: I consider it a great pleasure to be here tonight and to have had the opportunity of listening to this splendid symposium. I wish to say that Dr. Stookey's address, on peripheral nerve injuries, is the best I have ever heard. Dr. Stookey, who had charge of the neurosurgical service at Fort Henry during World War I, has done a great deal of work on peripheral nerve injuries and has contributed a fine monograph.

I was interested in hearing his historical review of the treatment of nerve injuries, especially what he had to say about Dr. Weir Mitchell, Dr. Keen and others; it is astonishing that since the days of the introduction of aseptic surgery and of Billroth and the development of all sorts of major surgery, even brain surgery, the surgery of the peripheral nerves has been so backward, even up to the first world war. A rather good textbook on surgery published in 1914 or 1915 advocated splicing the nerve by merely turning down a portion of it, just as in a tendoplasty. I think all that is known about peripheral nerve surgery dates from the last war. I believe that the experience of the surgeons in charge of the various hospitals in that war was about the same. They saw about the same things. They performed about the same operations and obtained about the same results, and I do not know of any one who had any particular, unusual tricks that permitted better regeneration of these nerves than any other man had. Knowledge seemed to be widespread, general, and their opinions were collective and in agreement.

I have little to add to Dr. Stookey's presentation; perhaps I might mention a few details which he did not have time to consider and of which he has seen hundreds of instances. All of us in the first world war were impressed with the much greater disability of the whole limb, as well as the greater local disability, in cases in which the blood vessel was injured, with the associated purplish tinge or plum color of the skin of the limb and, in the case of the arm, the tapering fingers. In such cases my associates and I obtained very poor results. The best result from a nerve suture that I ever saw was in a case in which we divided the ulnar nerve beneath the hypothenar eminence into its two branches so that we could suture the motor and the sensory division separately. I cannot give any statistics and shall only mention my impressions and recollections of our worst injuries. They were the major injuries of the brachial plexus, and in cases of such lesions an attempt was made to free and suture the trunk, which sometimes could hardly be found.

Neurolysis of a brachial plexus gave poor results in our hands.

In general, practically the only good result we obtained was in cases in which the nerves could be sutured together, end to end, without tension, and in fairly decent tissue, with proper splinting. If the suture was not accomplished under those conditions, we did not expect a good result, and we did not get it. That does not mean we got no good results with our sutures, for some were rather good, some were fair, some were middling but some were poor. Perhaps the best results were obtained with the musculospiral and the radial nerve, possibly because these nerves are chiefly motor. The poorest results were obtained with the brachial plexus, and we got fair results with the median, the musculocutaneous, the ulnar and the sciatic nerve and its branches. In some cases, because of loss of substance, the nerve ends can be brought together only by transposition. Only once, in a case in which the ulnar, median and musculocutaneous nerves were divided, with considerable separation of the ends, did Dr. Frazier seem unable to bring the ends together except by resection of the humerus. He resected about 3 or 4 inches (7.5 to 10 cm.) of the humerus of the extremity involved and was able to approximate the ends of these nerves nicely. I cannot tell you about the final result, because I was not able to follow the case.

I should like to make a commendatory remark about our brace department. Dr. Robin Buerki devised some simple and very efficient splints, which prevented paralyzed muscles from becoming overstretched. Another phase of the work which I should like to commend was the splendid occupational and physical therapy department at Fox Hills, where the good women worked day in and out, for weeks and months, encouraging the patients to have confidence, courage and faith.

Dr. Stookey's comments on grafts are pertinent. We had only 6 cases in which grafting was done. In each instance there was also major destruction of the soft parts. The nerves could not be brought together; so trellis grafts were used. The massive scar tissue resulting from healing of wounds with such gross destruction of soft parts, in which the grafts were placed, probably choked off the grafts and prevented downward growth of the nerve fibers. This fact no doubt accounted for the poor results. All the grafting was done by Dr. Frazier.

The establishment of a nerve bank, of which Dr. Stookey spoke, making available longer nerve sections, by which the gross areas of scar tissue could be bypassed, might permit better results.

I enjoyed Dr. Davis' paper—an authoritative paper—and he can speak authoritatively. His opinions are not mere hearsay, for he was a member of a committee which visited various battle fronts and obtained his information firsthand. I agree with every word he said except that I think the removal of a mosaic of bone, such as Dr. Cushing advocated in the last war, might be of use with certain injuries.

For treatment of infection of the brain substance of several days' duration, a Mikulicz tampon of penicillin gauze or iodoform gauze, as we have used it in infected, necrotic and purulent wounds of the brain which were not yet abscessed, has worked out very well. I should like to ask Dr. Davis about the intrathecal use of penicillin, for instance, when the ventricle has been perforated and there is gross infection of the brain. The results of treatment of various types of meningitis with penicillin is known, but I have not heard any one speak with authority on treatment of the perforated wounds of the ventricle with this substance.

I should like also to ask Dr. Davis whether Cobb Pelcher's work on animals in which he used various types of sulfonamide drugs and found that some were injurious to the brain tissue has been borne out by experience in the war.

I am unable to discuss Colonel Klingman's paper intelligently, but I am glad to have heard it. I am glad to hear of the great lengths to which the Medical Department has gone in this war to get men with cranial injuries out and around. I must say that our attitude in the last war was that a man who had been shot in the head was not quite, but almost, relegated thereafter to the world of useless people. The men were not encouraged to overcome their disability to the extent that they are now. The veterans' hospitals are still full of these poor fellows.

DR. JEFFERSON BROWDER, Brooklyn: I should like to point out that facial nerve grafts will heal even if the wound is infected. I have had experience with cases of this condition. It seems to me that considerable information might be derived from a more careful study of such cases. With respect to peripheral nerve injuries, my personal observation has been that, although a graft may not serve as a channel for the downgrowth of somatic nerve fibers, it will serve as a bridge for the downgrowth of sympathetic fibers. That is exceedingly important, particularly with the tibial nerves. I have had experience with cases in which, after a graft, ulceration of the sole of a foot healed and remained healed, although one could not demonstrate any return in somatic function. So even if one is defeated on one score, a graft of this character serves a useful purpose.

I should like to ask Dr. Davis a question in conjunction with Dr. King's: It is true that the purpose of all definitive treatment of open wounds of the brain is to convert them into closed wounds. If the operation can be carried out without infection, there is only the general cerebral insult to be dealt with thereafter. What has been the recent attitude toward wounds that break open after they have been closed primarily? Certainly, some of them do break open and require further consideration.

Dr. Klingman spoke of shock in association with trauma to the brain. It has been my experience that the so-called shock associated with cerebral injury, exclusive of the shock resulting from hemorrhage or injury to other parts, is not true shock; in other words, it is not characterized by the rapid pulse, the low pressure and the pallor and sweating. It is observed as pallor and sweating without the acceleration of pulse and often without reduction in arterial pressure. I should like to ask Dr. Klingman whether he has similarly observed that the shock associated with cerebral trauma without complicating factors, such as hemorrhage and injuries to the extremities, has been as I have stated.

DR. LOYAL DAVIS, Chicago: In answer to Dr. King's question: To my knowledge, the only results of the use of penicillin for craniocerebral injuries are those carried out by Cairns and Florey in Sicily in the treatment of about 200 men with combined craniocerebral injuries. As far as I know, the report of their work has not yet been published. However, I observed the use of penicillin injected intrathecally and introduced into the ventricle in a case of meningitis following a combined craniocerebral injury. The results were remarkable, in view of the fact the condition was resistant to the sulfonamide drugs. The statement that I made about sulfathiazole therapy came from Ascroft, who used the drug in the Middle East without the ill effects which other investigators have reported. In answer to Dr.

Browder, I closed wound from infection followed by However, secondary wounds located secondary
LIEUT. C. Army of various diseases Dr. Browder

Browder, I can only say that I have seen primarily closed wounds, clinically cleansed wounds, break down from infection and then make a secondary closure, followed by satisfactory healing without suppuration. However, sulfonamide compounds were used in the wounds locally and given by mouth at the time of the secondary closure.

LIEUT. COL. WALTER KLINGMAN, Medical Corps, Army of the United States: I wish to thank the various discussers for their comments. In reply to Dr. Browder's question about the nature of the shock,

I must confess that my military experience with shock has been confined chiefly to the accidents which have to do with flying. As you know, such accidents are probably the most violent of physical injuries, and many of them are associated with fractures or injuries in parts other than the head. However, it has been my experience in cases in which there has been simple head trauma, with no other fractures or injuries that could be responsible for surgical shock, as it is understood, that there is sometimes no apparent relationship between the disturbance of consciousness and the presence of what is ordinarily described as surgical shock.

Book Reviews

François Magendie: Pioneer in Experimental Physiology and Scientific Medicine in XIX Century France. By J. M. B. Olmsted, Professor of Physiology, University of California. With a preface by John F. Fulton, M.D. Price, \$5. Pp. 290, with 5 illustrations. New York: Schuman's, 1944.

François Magendie was born in 1783 and lived through the dramatic events in France of the French Revolution and the Napoleonic Era, a course of events which had great importance in shaping his life. His father, a surgeon, was imbued with the strong liberal views of his time. He attempted to apply the principles of Rousseau to the educational development of his children. It may be that his early discipline and his freedom from restraint were transformed in later life to impulsive frankness, which often went too far in its vigorousness.

After Magendie obtained his medical degree, he wrote a scientific thesis which became the cornerstone for his future medical thinking and research. In this thesis he attacked the theories of Bichat. Bichat propounded the idea that an organism is imbued with "vital properties" and that the essence of these "vital properties" is that they are changeable and not measurable. Magendie attempted to show that "vital properties" can be measured and that the organism can be subjected to experimental methods.

One of his first researches was to experiment on animals with a poison used by natives on the tips of arrows, and he described the effects, the convulsions, the vomiting and the final death of the animal. He showed that the pharmacologic effect was mediated through the spinal cord. This, of course, is now known to be the strychnine effect. He employed many techniques that are still in use today in pharmacologic and physiologic work. He used the technic of the isolated limb, the technic of crossed circulation and the technic of intravenous injection below a ligature. On the basis of work, he became known as the father of experimental pharmacology. He wrote a textbook of physiology in 1816, which was well received and contained information that he had derived from his own work. Some of the material in it, however, is curious, although undoubtedly true, such as "The more voluminous the buttocks and the more they are charged with fat, the greater will be the solidity of the sitting posture." He was the first to use rodents for nutritional experiments. He collaborated with a chemist in the discovery of emetine. His passion for experiment and his search for knowledge were so great that they frequently led him into strange pathways; for example, some curious experiments are described by him on the chemical analysis of intestinal gases of four executed prisoners who had dieted on bread, cheese and red wine.

In 1821 he wrote his famous formulary. He described a list of drugs and their effects in experimental situations and on human subjects, together with dosage and therapeutic uses. The book was three hundred pages long and was the forerunner of the more modern formularies.

Academic recognition came later to him than deserved. This was due chiefly to his propensity for developing strong opposition. As he grew older, his characteristics of outspoken frankness and of aggressiveness became more marked. When he believed that certain things were wrong, he said so openly. When he himself was attacked, he defended himself warmly and gave vigorous counterblows. As a result, no one could have a neutral attitude toward him. Either he was greatly admired and respected or he was roundly hated and feared.

Later in his life Magendie devoted his work exclusively to the central nervous system. He described decerebrate rigidity, circus movements as a result of cerebellar injury and the foramen of Magendie.

Some of his observations, however, were faulty, such as attributing vision to the fifth nerve because of the lack of blink response and stating that the function of the pineal gland was to open and close the aqueduct of Sylvius.

The famous controversy between Bell and Magendie over the discovery of the function of the anterior and posterior roots is of historical interest. This controversy agitated French and English medicine for a decade, and every once in a while there is still an eruption, with a review of the factors involved.

Magendie had a healthy skepticism, which he applied to the therapeutic procedures of his day. He scoffed at "shotgun" prescriptions, and he derided blood-letting therapy. His point of view is well illustrated by the introduction that he wrote on becoming the editor of a journal. He stated, "Nothing is more harmful to the progress of medicine than the absurd isolation which the majority of physicians use to maintain with respect to the natural sciences. . . ."

One of his most famous pupils was Claude Bernard, who succeeded him to the professorship of medicine at the College of France. Claude Bernard said that Magendie loved to assume a certain aggressiveness, particularly toward younger members of his profession. He would always contradict what they told him. He wanted the young men to persist in their points of view and ultimately to demonstrate the truth of their assertions. If the truth were so demonstrated, Magendie was always willing to listen and to accept the facts.

Magendie was married in 1830. Unfortunately, the author reveals little about his personal life and his emotional reactions of a more intimate nature. The readers of today, who are accustomed to the modern historical novel and the psychoanalytic biography, will miss anecdotes and will miss sufficient personal detail to build up a picture of Magendie as a man. However, one obtains from the book a good deal of the scene of France of the day and some smattering of a historical background.

The book is interestingly written and very readable. It is evident that a good deal of research and scholarship has gone into compiling the data.

As a historical review of the scientific life of Magendie the book is well recommended.

INDEX TO VOLUME 54

The asterisk (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.

Abnormalities and Deformities: See Twins; and under names of diseases, organs and regions, as Atlas and Axis; Ribs; Spine; etc.

Abscess: See under names of organs and regions, as Brain, abscess; etc.

Accidents: See Trauma

Acetylase: See Enzymes

Acetyl-Beta-Methylcholine: See Choline and Choline Derivatives

Acetylcholine: See Choline and Choline Derivatives

Acid, lactic, oxidation quotient in minced brain of normal and avitaminotic chicken, 418

Adenohypophysis: See Pituitary Body

Adiposity: See Obesity

Adiposogenital Syndrome: See under Pituitary Body

Adrenal Preparations: effect of intravenous injection of epinephrine and angiotonin before and after production of neurogenic hypertension, 418
emotions and adrenergic and cholinergic changes in blood, *110

Adrenalectomy: See under Adrenals

Adrenals, effect of adrenalectomy on brain of white rats, 429
inhibition of histamine release by pituitary-adrenal mechanism, 422

Aerobautics: See Aviation and Aviators

After-Image: See Vision

Age, incidence of advanced maternal age in mothers of 1,000 state hospital patients, *186
multiple sclerosis with late onset of symptoms, *348
Old: See Old Age

Air, Pressure: See also Altitude; Aviation and Aviators
pressure; comparison of altitude and exercise with respect to decompression sickness, 420
studies on cerebral edema; reaction of brain to air exposure; pathologic changes, *163
studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290

Albinism, partial, and nystagmus in Negroes, 156

Alcoholism: See Delirium tremens

Allergy: See Anaphylaxis and Allergy

Alpers, B. J.: Arteriovenous aneurysm of great cerebral vein and arteries of circle of Willis; formation by junction of great cerebral vein and straight sinus and by choroidal arteries and anomalous branches of posterior cerebral arteries, *181

Alpha Tocopherol, Therapy: See Dystrophy, muscular

Altitude: See also Air, pressure
comparison of altitude and exercise with respect to decompression sickness, 420
High: See Aviation and Aviators

Altschul, R.: Otto Sittig, 303

Amaurosis: See Blindness

Amblyopia: See Blindness

Amebiasis; amebic colitis complicated with abscess of brain, 152

Amentia: See Insanity; Mental Diseases; etc.

Amphetamine; psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amylal and amphetamine sulfate, *372

Amputation; limb parameters and regression rates in denervated amputated limbs of Urodele larvae, 419

Analgesia: See Anesthesia; Pain

Anaphylaxis and Allergy: See also Schwartzman Phenomenon; etc.
allergic brain changes in post-scarlatinal encephalitis, 152

Anemia, Cerebral: See Brain, blood supply
pernicious degeneration of peripheral nerves in, *102
pyridoxine deficiency in swine, with reference to anemia, epileptiform convulsions and fatty liver, 305

Anesthesia, acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
preliminary report on method for lengthening effect of sympathetic nerve block, 61
studies on flying personnel with operational fatigue; modification of pentothal therapy, 229

Anesthetics: See Anesthesia

Aneurysm, arteriovenous, of great cerebral vein and arteries of circle of Willis; formation by junction of great cerebral vein and straight sinus and by choroidal arteries and anomalous branches of anterior cerebral arteries, *181
arteriovenous, of midbrain and retina, facial nevi and mental changes, 154
congenital arterial aneurysm at papilla, 426

Angioma, cavernous, of medulla, 310

Angiotonin, effect of intravenous injection of epinephrine and angiotonin before and after production of neurogenic hypertension, 418

Anhydrase: See Blood, enzymes; Enzymes

Anomalies: See under names of organs and regions

Anorexia Nervosa: See Appetite

Anoxia: See Oxygen, deficiency

Anxiety: See also Neuroses and Psychoneuroses
hypothalamic attacks with thalamic lesion; physiologic and psychologic considerations, *37
psychologic factors in problem of obesity, 157

Apoplexy: See Brain, hemorrhage

Appetite, anorexia nervosa; metabolism and its relation to psychopathologic reactions, 424
bulimia associated with epilepsy in children, 427

Arlieff, A. J.: Use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of peripheral nerves, 317

Aring, C. D.: Hypothalamic attacks with thalamic lesion; anatomic considerations, *44
Hypothalamic attacks with thalamic lesion; physiologic and psychologic considerations, *37

Armed Forces Personnel: See also Aviation and Aviators; Military Medicine; Naval Medicine; Soldiers; Veterans; etc.
etiologic factors in adjustment of men in armed forces, 309

Arms: See also Extremities; etc.
brachial pain from herniation of cervical intervertebral disk, 60

Arsenic and Arsenic Compounds; hemorrhagic encephalopathy following 5 day treatment of early syphilis with massive doses of oxophenarsine hydrochloride (maparsen); report of case with recovery, 65
Therapy: See Syphilis

- Arteries: See also Aneurysm; Blood pressure; Periarthritis; Thrombosis; Vasomotor System; etc.
arteriovenous aneurysm of great cerebral vein and arteries of circle of Willis; formation by junction of great cerebral vein and straight sinus and by choroidal arteries and anomalous branches of anterior cerebral arteries, *181
Cerebral: See Brain, blood supply
- Arteritis: See Periarthritis
- Artificial Fever Therapy: See Neurosyphilis
- Asthenia, neurocirculatory, etiology and pathogenesis; hyperthermia as one of manifestations, 426
- Astrocystoma, normal air encephalograms in patients with convulsive seizures and tumor of brain, 62
- Atkinson, M.: Ménière's syndrome; comparison of results of medical and surgical treatment, *192
- Atlas and Axis, abnormalities; platybasia (basilar impression) secondary to advanced osteitis deformans (Paget's disease) with severe neurologic manifestations; successful surgical result; report of case, 68
- Atmosphere: See Air
- Atopy: See Anaphylaxis and Allergy
- Atrophy: See also under names of organs and regions, as Face; etc.
Muscular: See also Dystrophy, muscular
muscular; abortive Fröhlich syndrome with disease of cerebellum and spinal cord, polydactyly and muscular atrophy; new syndrome (?), 432
muscular; investigations on muscle atrophies arising from disuse and tenotomy, 421
muscular, progressive, histopathologic characteristics of, 317
- Audition: See Hearing
- Avery, L. W.: Common factors precipitating mental symptoms in aged, 312
- Aviation and Aviators: See also Air, pressure
acute high altitude anoxia, 421
high altitude frostbite, 221
studies on flying personnel with operational fatigue; modification of pentothal therapy, 229
- Avitaminoses: See under Vitamins
- Axis: See Atlas and Axis
- Axons: See Neurons
- Bacilli: See Bacteria
- Bacteria: See also Meningococci; Staphylococci; etc.
pyocyaneus; meningitis due to *Ps. pyocyanea*; penetrating wounds of head, 222
- Baker, A. B.: Central nervous system in uremia; clinicopathologic study, *130
- Bakody, J. T.: Traumatic glossopharyngeal neuralgia, 166
- Balser, B. H.: Studies on flying personnel with operational fatigue; modification of pentothal therapy, 229
- Barbital and Barbital Derivatives; acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amylal and amphetamine sulfate, *372
Therapy: See Mental Diseases
- Bardet-Laurence-Biedl Syndrome: See Laurence-Moon-Biedl Syndrome
- Barrier, Hemoencephalic: See Hemoencephalic Barrier
- Barry, H., Jr.: Incidence of advanced maternal age in mothers of 1,000 state hospital patients, *186
- Basilar Impression: See Atlas and Axis; Occipital Bone
- Behavior, Children's: See under Children
man's frontal lobes; critical review, *10
- Bender, M. B.: Extinction and precipitation of cutaneous sensations, *1
Localizing value of vertical nystagmus, *378
Polyopia and monocular diplopia of cerebral origin, *323
- Benton, A. L.: Visual retention test for clinical use, *212
- Benzedrine: See Amphetamine
- Berger Rhythm: See Brain, electroencephalography
- Biedl-Laurence Syndrome: See Laurence-Moon-Biedl Syndrome
- Birth, Illegitimate: See Illegitimacy
- Bismuth and Bismuth Compounds, Therapy: See Syphilis
- Blast: See Explosions
- Blindness: See also Vision
acute cortical blindness with recovery; report of case, 70
apperceptive, in Lissauer's dementia paralytica, 58
- Blood, bromide; incidence of bromism at Warren State Hospital, 217
- Circulation: See Arteries; Capillaries; Cardiovascular System; Heart; Vasomotor System; Veins; etc.
Diseases: See Anemia; etc.
emotions and adrenergic and cholinergic changes in, *110
enzymes; determination of carbonic anhydrase in human autopsy tissue, 306
iodine; thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
pressure, high; changes in cerebral veins in hypertensive brain disease and relation to cerebral hemorrhage; clinical pathologic study, *395
pressure, high; effect of intravenous injection of epinephrine and angiotonin before and after production of neurogenic hypertension, 418
pressure; immediate circulatory and respiratory effects of convulsive shock, 57
- Vessels: See Arteries; Capillaries; Cardiovascular System; Periarthritis; Vasomotor System; Veins; etc.
- Blood-Brain Barrier: See Hemoencephalic Barrier
- Blumenfeld, C. M.: Disseminated oligodendroglioma, *274
- Body, diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
- Bones: See also under names of bones
diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
Diseases: See Osteitis; etc.
- BOOK REVIEWS:
Basis of Clinical Neurology; S. Brock, 230
Bibliography of Visual Literature, 1939-1944; J. Fulton, P. M. Hoff and H. T. Perkins, 318
Cultural Background of Personality; R. Linton, 74
Examination of Reflexes: Simplification; R. Wartenberg, 73
François Magendie: Pioneer in Experimental Physiology and Scientific in XIX Century France; J. M. B. Olmsted, 442
Handbook of Psychiatry; L. J. Karnosh and E. M. Zucker, 156
Large Scale Rorschach Techniques: Manual for Group Rorschach and Multiple Choice Test; M. R. Harrower-Erickson and M. E. Steiner, 72
Psychology of Women: Motherhood; H. Deutsch, 318
Story of Hospital; C. A. Elsberg, 73
- Bouillaud's Disease; See Rheumatic Fever
- Boutons: See Nerves, roots

Brachial Plexus: See Paralysis
Brachium Pontis: See Cerebellum
Brain: See also Cerebellum; Corpus Callosum; Corpus Striatum; Hypothalamus; Medulla Oblongata; Meninges; Nervous System; Thalamus; etc.
 abscess, amebic colitis complicated with, 152
 abscess; rupture of left temporosphenoidal brain abscess into ventricle, 58
 acute and chronic parietal lobe ablations in monkeys, 420
 acute cortical blindness with recovery; report of case, 70
Blood Supply: See also Aneurysm; Arteries; Hemoencephalic Barrier; Thrombosis; etc.
 blood supply; arteriovenous aneurysm of great cerebral vein and arteries of circle of Willis; formation by junction of great cerebral vein and straight sinus and by choroidal arteries and anomalous branches of anterior cerebral arteries, *181
 blood supply; cerebral thromboangitis obliterans and its relation to periarthritis nodosa, 219
 cavernous sinus thrombophlebitis: report of case with multiple cerebral infarcts and necrosis of pituitary body, 153
 cerebral metabolism in experimental head injury, 420
 changes in alcoholic psychoses, 220
 changes in electrical activity of cortex due to applications of acetylcholine, 71
Concussion: See Brain, injuries
 course of striate medullares in human brain, 304
 cysts; chemistry of cerebral tumors and of cerebral cyst fluids, 151
 cysts, congenital, in left temporal lobe, 59
 cysts; experimental traumatic cerebral cysts in rabbit, 58
 cysts; porencephaly; studies in phlebothrombosis and phlebostasis, 219
Diseases: See also Encephalitis; Insanity; Mental Diseases; etc.
 diseases; late cerebral sequelae of rheumatic fever, 151
 disturbances in sleep mechanism; clinicopathologic study; lesions at corticodiencephalic level, *241
 edema, experimental; cerebral circulation, 307
 edema, experimental; methods of producing, 218
 edema; reaction of brain to air exposure; pathologic changes, *163
 edema; reaction of brain to exposure to air; physiologic changes, *290
 effect of adrenalectomy on brain of white rats, 429
 electroencephalogram of dogs with experimental space-occupying intracranial lesions, *141
 electroencephalographic localization and differentiation of lesions of frontal lobes; pathologic confirmation, *197
 electroencephalography; parasympathetic regulation of high potential in electroencephalogram, 419
 experimental investigation of connections between corpus striatum and substantia nigra in cat, 304
 extinction and precipitation of cutaneous sensations, *1
 hemorrhage; changes in cerebral veins in hypertensive brain disease and relation to cerebral hemorrhage; clinical pathologic study, *395
 hemorrhagic encephalopathy following 5 day treatment of early syphilis with massive doses of oxophenarsine hydrochloride (mapharsen); report of case with recovery, 65
 hernia; mechanics of trauma with reference to herniation of cerebral tissue, 57
 human pyramidal tract; study of pyramids in cases of acute and chronic vascular lesions of brain, *339
Inflammation: See Encephalitis
Injuries: See also Cranium, injuries; Head, injuries
 injuries; blast injury; nonfatal case with neurologic signs, 155
 injuries; experimental traumatic cerebral cysts in rabbit, 58
 injuries; traumatic dilatation of cerebral ventricles, 58

Brain—Continued

lactic acid oxidation quotient in minced brain of normal and avitaminotic chicken, 418
 lesions associated with experimental "epileptiform" seizures in monkey, 154
Localization of function: See also Brain, diseases; Brain, pathology; Brain, tumors
 localization of function; midbrain auditory mechanisms in cats, 306
 localization of function; paralysis with hypotonicity and hyperreflexia subsequent to section of basis pedunculi in monkeys, 218
 localization of function; receiving areas of tactile, auditory and visual systems in cerebellum, 217
 man's frontal lobes; critical review, *10
 multiplicity of representation versus punctate localization in motor cortex; experimental investigation, *256
 of *Drosophila melanogaster*, 417
 oxidation of fructose by brain in vitro, 306
 pathology; relation of cerebral cortex to spasticity and flaccidity, 420
 physiologic effects of bilateral simultaneous frontal lesions in primate, 304
Physiology: See also Brain, electroencephalography; Brain, localization of function
 physiology; spreading depression of activity in cerebral cortex, 218
 pia circulation and spreading depression of activity in cerebral cortex, 306
 polyopia and monocular diplopia of cerebral origin, *323
 propagation of epileptiform impulses in brain; role of corpus callosum, 151
 reactions of monkeys of various ages to partial and complete decortication, 57
Sclerosis: See Sclerosis
 studies of action of acetylcholine on motor cortex; correlation of effects of acetylcholine and epilepsay, *391
 tumors; chemistry of cerebral tumors and of cerebral cyst fluids, 151
 tumors; disseminated oligodendroglioma, *274
 tumors; intracranial lipoma, 423
 tumors; localizing value of temporal crescent defects in visual fields, *97
 tumors; normal air encephalograms in patients with convulsive seizures and tumor of brain, 62
 tumors; paroxysmal and postural headaches from intraventricular cysts and tumors, 155
 tumors; spinal fluid in metastatic brain tumors, 223
 water, nitrogen, and electrolyte concentration in, 306
Brazier, M. A. B.: Tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
Breast, cancer: paralysis of larynx; early sign of recurrence following radical mastectomy for carcinoma, 429
Brenner, C.: Experimental evidence of physiologic mechanism of certain types of headache, *385
Bromide and Bromine: incidence of bromism at Warren State Hospital, 217
Bulimia: See under Appetite
Bullet Wounds: See under Wounds
Bywater, W. G.: Anticonvulsant activity of sulfides and sulfones, *319
Cancer: See also Tumors; etc.; and under names of organs and regions
 metastases; paralysis of larynx; early sign of recurrence following radical mastectomy for carcinoma, 429
 neurosurgery and radiation for relief of pain in advanced cancer, 431
Candida: See Moniliasis
Capillaries: See also Vasomotor System
 of finger nail folds in cases of neurosis, epilepsy and migraine, 225
 permeability; studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290
Carbaminoylecholine: See Choline and Choline Derivatives

- Carbonic Anhydrase: See Blood, enzymes; Enzymes
- Cardiovascular System: See also Arteries; Vaso-motor System; etc.
variation in circulatory and respiratory responses to carotid sinus stimulation in man, 418
- Carotid Sinus: variation in circulatory and respiratory responses to carotid sinus stimulation in man, 418
- Casamajor, L.: Smith Ely Jelliffe, 301
- Case, T. J.: Effects of penicillin on central nervous system, 160
- Catatonia: See Dementia Precox
- Cauda Equina: See Spinal Cord
- Caudate Nucleus: See Corpus Striatum
- Causalgia: See Neuralgia
- Cavernous Sinus, Thrombophlebitis: See Thrombosis
- Cells: See Neurons; Tissue; etc.
- Cephalalgia: See Headache
- Cephalocele: See Brain, hernia
- Cerebellum, abortive Fröhlich syndrome with disease of cerebellum and spinal cord, polydactyly and muscular atrophy; new syndrome (?), 432
function of anterior cerebellar lobe, 227
Localization of Function: See Brain, localization of function
- Cerebrospinal Fever: See Meningitis
- Cerebrospinal Fluid; excretion of penicillin in spinal fluid in meningitis, 62
in closed head injuries, 155
in metastatic brain tumors, 223
treatment of rhinorrhea and otorrhea, 430
- Cerebrum: See Brain
- Chemotherapy: See Dementia Paralytica; Meningitis
- Children, bulimia associated with epilepsy in, 427
schizophrenia in 4 year old boy, 425
- Chlorides; salt metabolism in poliomyelitis, 57
- Choanae: See Nose
- Choked Disk: See Neuritis, optic
- Choline and Choline Derivatives: See also Cholin-esterase
changes in electrical activity of cortex due to applications of acetylcholine, 71
effects of acetyl-beta-methylcholine in human subjects with localized lesions of central nervous system, 217
emotions and adrenergic and cholinergic changes in blood, *110
formation of acetylcholine; new enzyme: "choline acetylase," 419
studies of action of acetylcholine on motor cortex; correlation of effects of acetylcholine and epilepsy, *391
- Cholinesterase, functional differentiation in embryonic development; cholinesterase activity of induced neural structures in *Amblystoma punctatum*, 418
- Chordoma; chordomata; review of literature, with report of sacrococcygeal case, 59
- Chordotomy: See Spinal Cord
- Circle of Willis: See Brain
- Circulatory System: See Cardiovascular System; Heart
- Circumolivary Fascicles: See Pyramidal Tract
- Civilization, some aspects of compulsion neurosis in changing civilization, 307
- Colitis, Amebic: See Amebiasis
- Coma: See Dementia Precox
- Communicable Diseases: See Meningitis; Syphilis; etc.
- Compulsion: See Dementia Precox; Neuroses and Psychoneuroses
- Concussion: See Brain, injuries
- Congress: See Societies
- Conjunctiva; diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
- Connor, G. J.: Function of anterior cerebellar lobe, 227
- Contusion: See Brain, injuries
- Convulsions: See also Epilepsy
anticonvulsant activity of sulfoxides and sulfones, *319
hysterical convulsions treated with hypnosis and psychotherapy; report of case, 314
- Corpus Callosum; propagation of epileptiform impulses in brain; role of corpus callosum, 151
- Corpus Luysi: See Hypothalamus
- Restiforme: See under Medulla Oblongata
- Corpus Striatum; experimental investigation of connections between corpus striatum and substantia nigra in cat, 304
- Correction in transcript of article by Dr. Silvano Arieti entitled "Primitive Habits and Perceptual Alterations in Terminal Stage of Schizophrenia" (*Arch. Neurol. & Psychiat.* 53: 378 [May] 1945), 74
- Corticospinal Tract: See Pyramidal Tract
- Cranial Venous Sinuses: See Lateral Sinus
- Cranium: See also Occipital Bone; Parietal Bone; etc.
diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
electroencephalogram of dogs with experimental space-occupying intracranial lesions, *141
Injuries: See Brain, injuries; Head, injuries
some considerations concerning roentgen diagnosis of skull fractures, 62
- Cryptococci Hominis: See Torula
- Curare, immediate circulatory and respiratory effects of convulsive shock, 57
- Cysts: See under names of organs and regions, as Brain; etc.
- DaCosta's Syndrome: See Asthenia, neurocirculatory
- Davis, L.: Management and treatment of cranio-cerebral injuries, 433
- Davidson, C.: Disturbances in sleep mechanism; clinicopathologic study; lesions at corticodiencephalic level, *241
Multiple sclerosis with late onset of symptoms, *348
- Deafness: See Ear; Hearing; etc.
- Decompression: See Air, pressure
- Dejerine-Roussy Syndrome: See Thalamus
- Delirium: See also Insanity
tremens; changes in brain in alcoholic psychoses, 220
tremens; tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
- Delusions: See under Dementia Precox; etc.
- Dementia: See Dementia Paralytica; Dementia Precox; Insanity; etc.
- Dementia Paralytica: See also Neurosyphilis
effects of penicillin on central nervous system, 160
experimental study on treatment with penicillin, 311
Lissauer's, apperceptive blindness in, 58
- Dementia Precox, acute excitement induced by electric shock therapy, 67
fatal catatonia, 424
psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amytal and amphetamine sulfate, *372
responses of schizophrenic patients to induced anoxia, 307
schizophrenia in 4 year old boy, 425
schizophrenic reaction syndrome in course of acute demyelination of central nervous system; clinicopathologic report of case, with brief review of literature, *202

- Demuth, E. L.: Disturbances in sleep mechanism; clinicopathologic study; lesions at corticodiencephalic level, *241
- Denny-Brown, D.: Effects of transient stretching of peripheral nerve, *116
- Depersonalization: See Personality
- Depression: See also Insanity; Mental Diseases; Neuroses and Psychoneuroses
psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amylal and amphetamine sulfate, *372
thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
- Dermatoses: See Skin, diseases
- Diencephalon: See Brain
- Diethelm, O.: Emotions and adrenergic and cholinergic changes in blood, *110
- Diethylstilbestrol: See Estrogens
- Diphtheria, central nervous system in, 152
- Diplegia: See Paralysis
- Diplopia, monocular, and polyopia of cerebral origin, *323
- Disk, Choked: See Neuritis, optic
- Optic: See Nerves, optic
- Intervertebral: See under Spine
- Dizziness: See Vertigo
- Di Alpha Tocopherol: See Vitamins, E
- Doherty, M. M.: Effects of transient stretching of peripheral nerve, *116
- Doty, E. J.: Emotions and adrenergic and cholinergic changes in blood, *110
- Drew, J. H.: Polycythemia as neurosurgical problem; review, with reports of 2 cases, *25
- Dropsy; cystic hydrops of pineal gland, 427
- Dublin, W.: Histopathologic characteristics of progressive muscular atrophy, 317
- Duodenum, Ulcers: See Peptic Ulcer
- Dyskinesia: See Movements
- Dyspluitarism: See Pituitary Body
- Dystonia: See Muscles, tonus
- Dystrophy, Adiposogenital: See under Pituitary Body
Muscular: See also Atrophy, muscular
muscular; myotonic dystrophy, 156
muscular, progressive, defect in utilization of tocopherol in, 218
- Ear: See also Hearing
discharge; treatment of rhinorrhea and otorrhea, 430
effect of anoxia on vestibular apparatus, 305
Internal: See Nerves; Nystagmus; Vertigo, aural; etc.
- Economics, Medical: new veteran and future for practice of medicine, 64
- Ectoderm, embryonic grafts in regenerating tissue: development of dorsal and ventral ectoderm of *Rana pipiens gastrulae*, 417
- Ectodermal Defect; hereditary ectodermal dysplasia, 156
- Edema: See under names of organs and regions, as Brain; etc.
- Education, postgraduate course in psychiatry, McGill University, 412
psychotherapy and public education, 159
University of California course in psychiatry, 412
- Effort Syndrome: See Asthenia, neurocirculatory
- Electricity: See Electrotherapy
- Electrodiagnosis: See Brain, electroencephalography; Heart; etc.
use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of peripheral nerves, 317
- Electroencephalogram: See Brain, electroencephalography
- Electrolytes, water and nitrogen concentration in brain, 306
- Electromyogram: See under Muscles
- Electronarcosis: See Anesthesia
- Electrotherapy: See also Epilepsy; Mental Diseases; etc.
acute excitement induced by electric shock therapy, 67
electroshock convulsion syndrome, 150
psychologic studies on patient who received 248 shock treatments, *409
- Embolism: See Thrombosis
- Emotions: See also Anxiety; etc.
and adrenergic and cholinergic changes in blood, *110
emotional trauma resulting from illegitimate birth, *381
psychologic factors in problem of obesity, 157
studies on palmar sweating, 217
- Encephalitis: See also Encephalomyelitis
affecting basal ganglia in monkeys, 219
allergic brain changes in post-scarlatinal encephalitis, 152
complicating virus pneumonia, 151
- Encephalocele: See Brain, hernia
- Encephalomalacia: See Brain, pathology
- Encephalomyelitis, acute meningococcal, 221
distinctive type occurring among troops in northern territory of Australia, 423
- Encephalopathy: See under Brain
- Encephalorrhagia: See Brain, hemorrhage
- Endocrine Therapy: See under names of glands and hormones, as Adrenal Preparations; Insulin
- Engel, G. L.: Hypothalamic attacks with thalamic lesion; anatomic considerations, *44
Hypothalamic attacks with thalamic lesions; physiologic and psychologic considerations, *37
- English, O. S.: Psychotherapy and public education, 159
- Entameba: See Amebiasis
- Enuresis: See Urination, incontinence
- Enzymes: See also under names of enzymes, as Cholinesterase; etc.
determination of carbonic anhydrase in human autopsy tissue, 306
formation of acetylcholine; new enzyme: "choline acetylase," 419
- Ependyma; ependymitis and meningitis due to *Candida* (Monilia) albicans; report of fatal case of meningitis with comment on its clinical, bacteriologic and pathologic aspects, *361
- Ephedrine: See Myasthenia Gravis
- Epidermis: See Skin
- Epilepsy: See also Convulsions
anticonvulsant activity of sulfoxides and sulfones, *319
associated with bulimia in children, 427
brain lesions associated with experimental "epileptiform" seizures in monkey, 154
capillaries of finger nail folds in cases of neurosis, epilepsy and migraine, 225
normal air encephalograms in patients with convulsive seizures and tumor of brain, 62
propagation of epileptiform impulses in brain; role of corpus callosum, 151
pyridoxine deficiency in swine, with reference to anemia, epileptiform convulsions and fatty liver, 305
studies of action of acetylcholine on motor cortex; correlation of effects of acetylcholine and epilepsy, *391
- Epinephrine: See Adrenal Preparations
- Epiphysis: See Pineal Gland
- Equilibrium: See Cerebellum; Nystagmus; Posture; etc.
- Erythremia: See Polycythemia
- Erythrocytes: See Anemia; Polycythemia; etc.
- Estrin: See Estrogens
- Estrogens, convulsive shock therapy in involutional states after complete failure with previous estrogenic treatment, 307
diethylstilbestrol in management of psychopathologic states in males, 430

- Ether: See Anesthesia
- Ethylstilbestrol: See Estrogens
- Evans, V. L.: Acute excitement induced by electric shock therapy, 67
- Excitement, acute, induced by electric shock therapy, 67
- Exercise; comparison of altitude and exercise with respect to decompression sickness, 420
- Exhaustion: See Fatigue
- Explosions; blast injury; nonfatal case with neurologic signs, 155
- Extremities: See also Arms
blood supply; high altitude frostbite, 221
blood supply of peripheral nerves; practical considerations, *280
injuries; post-traumatic pain and causalgic syndrome, 61
limb parameters and regression rates in denervated amputated limbs of Urodele larvae, 419
Paralysis: See Paralysis; Poliomyelitis
- Eyes: See also Vision; and under special structures of eyes
Movements: See under Encephalitis; Eyes, paralysis; Nystagmus; etc.
paralysis; unilateral internal ophthalmoplegia; sole clinical sign in patient with syphilitic meningitis, *389
toxoplasmosis; report of ocular findings in infant twins, 223
- Fabing, H. D.: Narcolepsy; combat experience of soldier with narcolepsy, *367
- Face, atrophy; progressive facial hemiatrophy, *75
- Fat in Liver: See under Liver
- Fatigue; studies on flying personnel with operational fatigue; modification of pentothal therapy, 229
- Feces, attempts to recover poliomyelitis virus from fruit, well water, chicken cords and dog stools, 429
- Feeling: See Emotions
- Fell-Klippel Syndrome: See Spine, abnormalities
- Feindel, W. H.: Studies on cerebral edema; reaction of brain to air exposure; pathologic changes, *163
Studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290
- Ferments: See Enzymes
- Fetus: See Pregnancy
- Fever: See also Malaria; Typhoid; etc.
etiology and pathogenesis of neurocirculatory asthenia; hyperthermia as one of manifestations of neurocirculatory asthenia, 426
hypothalamic attacks with thalamic lesion; anatomic considerations, *44
hypothalamic attacks with thalamic lesion; physiologic and psychologic considerations, *37
Therapeutic: See Dementia Paralytica; Mental Diseases; Neurosyphilis; etc.
- Filum Terminale: See Spinal Cord
- Finger Nails: See Nails
- Fodor, N.: Emotional trauma resulting from illegitimate birth, *381
- Foramen, Intervertebral: See under Spine
- Magnum: See Medulla Oblongata
- Forster, F. M.: Arteriovenous aneurysm of great cerebral vein and arteries of circle of Willis; formation by junction of great cerebral vein and straight sinus and by choroidal arteries and anomalous branches of anterior cerebral arteries, *181
Changes in electrical activity of cortex due to applications of acetylcholine, 71
Studies of action of acetylcholine on motor cortex; correlation of effects of acetylcholine and epilepsy, *391
- Foster, D. B.: Degeneration of peripheral nerves in pernicious anemia, *102
- Fractures: See under names of bones and joints, as Cranium; etc.
- Freidinger, A. W.: Psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amytal and amphetamine sulfate, *372
- Friedman, A. P.: Experimental evidence of physiologic mechanism of certain types of headache, *385
Multiple sclerosis with late onset of symptoms, *348
- Fröhlich Syndrome: See Pituitary Body
- Frostbite; high altitude frostbite, 221
- Fructose: See Levulose
- Fruit, attempts to recover poliomyelitis virus from fruit, well water, chicken cords and dog stools, 429
- Ganglion: See Nervous System; Neurons
Basal: See Encephalitis
- Gardner, W. J.: Disseminated oligodendroglioma, *274
- Gastric Ulcer: See Peptic Ulcer
- Gellhorn, E.: Multiplicity of representation versus punctate localization in motor cortex; experimental investigation, *256
- Genitals: See under names of genitals
- Geriatrics: See Old Age
- Golseth, J. G.: Use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of peripheral nerves, 317
- Gonadotropins: See also Pituitary Body
chorionic; Simmonds' disease with therapeutic response to hormone therapy for 4 years; report of case with necropsy findings, 151
- Gottlieb, J. S.: Psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amytal and amphetamine sulfate, *372
- Graduate Work: See Education
- Grant, F. C.: Curious lesions of spinal cord; report of 2 cases, 226
Polycythemia as neurosurgical problem; review, with reports of 2 cases, *25
- Granuloma, Malignant: See Hodgkin's Disease
- Hallucinations: See Delirium
- Hassin, G. B.: Histopathologic characteristics of progressive muscular atrophy, 317
- Hauptmann, A.: Capillaries of finger nail folds in cases of neurosis, epilepsy and migraine, 225
- Head: See also Cranium
injuries: See also Brain, injuries; Cranium, injuries; etc.
injuries; cerebral metabolism in experimental head injury, 420
injuries; cranio-cerebral wounds; exteriorization method of treatment, 429
injuries, intellectual impairment in, 220
injuries; management and treatment of cranio-cerebral injuries, 433
injuries; meningitis due to Ps. pyocyanea; penetrating wounds of head, 222
injuries; 1 aspect of post-traumatic syndrome in cranio-cerebral injuries, 223
injuries; spinal fluid in closed head injuries, 155
injuries; traumatic pneumocephalus with spontaneous ventriculograms, 58
- Headache: See also Migraine
experimental evidence of physiologic mechanism of certain types of, *385
paroxysmal and postural headaches from intraventricular cysts and tumors, 155
- Hearing, midbrain auditory mechanisms in cats, 306
- Hebb, D. O.: Man's frontal lobes; critical review, *10
- Hebephrenia: See Dementia Precox
- Hellbrunn, G.: Experimental study on treatment of dementia paralytica with penicillin, 311
Hemorrhagic encephalopathy following 5 day treatment of early syphilis with massive doses of oxophenarsine hydrochloride (mapharsen); report of case with recovery, 65

- Heine-Medin's Disease: See Poliomyelitis
- Hematology: See Blood
- Hemiatrophy: See Face, atrophy
- Hemiplegia: See also Paralysis
human pyramidal tract; study of pyramids in cases of acute and chronic vascular lesions of brain, *339
- Hemoencephalic Barrier: experimental study on treatment of dementia paralytica with penicillin, 311
- Hemorrhage: See Brain; Eyes; Larynx; Spinal Cord; etc.
- Hernia: See Brain
- Hip, tabetic arthropathy of, 62
- Histamine, experimental evidence of physiologic mechanism of certain types of headache, *385
inhibition of histamine release by pituitary-adrenal mechanism, 422
- Hodgkin's Disease, binocular papilledema in case of torulosis associated with, 426
- Hoffenberg, N. L.: Hemorrhagic encephalopathy following 5 day treatment of early syphilis with massive doses of oxophenarsine hydrochloride (mapharsen); report of case with recovery, 65
- Hormones: See Adrenal Preparations; Estrogens; Gonadotropins; Insulin; etc.
- Hospitals, incidence of advanced maternal age in mothers of 1,000 state hospital patients, *186
incidence of bromism at Warren State Hospital, 217
group psychotherapy in mental institutions, 64
- Hydrogen Ion Concentration: See also Cerebrospinal Fluid; etc.
studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290
- Hydrops: See Dropsy
- Hyperhidrosis: See Sweat Glands
- Hyperinsulinism: See under Insulin
- Hypersomnia: See Sleep
- Hypertension: See Blood pressure, high
- Hyperthermia: See Fever
- Hypertrophy: See under names of organs and regions
- Hypnosis, hysterical convulsions treated with hypnosis and psychotherapy; report of case, 314
- Hypoglycemia: See Blood sugar; Insulin
- Hypomania: See Mental Diseases
- Hypophysectomy: See under Pituitary Body
- Hypophysis: See Pituitary Body
- Hypopituitarism: See Pituitary Body
- Hypothalamus: See also Pituitary Body
hypothalamic attacks with thalamic lesion; anatomic considerations, *44
hypothalamic attacks with thalamic lesion; physiologic and psychologic considerations, *37
- Hysteria: See also Neuroses and Psychoneuroses
"acting out" as defense mechanism; report of case, 159
hysterical convulsions treated with hypnosis and psychotherapy; report of case, 314
- Icterus: See Jaundice
- Illegitimacy; emotional trauma resulting from illegitimate birth, *381
- Inductee: See Recruits
- Infantile Paralysis: See Poliomyelitis
- Infantilism, Pituitary: See under Pituitary Body
- Infants: See also Children
newborn; kernicterus unassociated with erythroblastosis fetalis, 423
- Infarction: See under Brain
- Infundibulum: See Hypothalamus
- Insanity: See also Dementia Precox; Depression; Mental Diseases
thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
- Insulin, migraine headaches relieved by hypoglycemic reaction, 61
- Intelligence, Tests: See Mental Tests
- Intervertebral Disks: See Spine, intervertebral disks
- Intoxication: See Bromide and Bromine
- Intradural Space: See Cranium
- Iodine and Iodine Compounds, in Blood: See Blood, iodine
- Jaundice, kernicterus unassociated with erythroblastosis fetalis, 423
- Johnson, H. C.: Effects of penicillin on central nervous system, 160
- Joints: See also under names of joints, as Hip; etc.
changes of weight and neuromuscular transmission in muscles of immobilized joints, 419
- Joseph, G. F.: Unilateral internal ophthalmoplegia; sole clinical sign in patient with syphilitic meningitis, *389
- Kahn, E.: Thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
- Kalz, G. G.: Ependymitis and meningitis due to *Candida (Monilia) albicans*; report of fatal case of meningitis, with comment on its clinical, bacteriologic and pathologic aspects, *361
- Klapman, J. W.: Group psychotherapy in mental institutions, 64
- Klingman, W. O.: Psychiatric aspects of injuries to nervous system, 437
- Klippel-Feil Syndrome: See Spine, abnormalities
- Knutson, J.: Central nervous system in uremia; clinicopathologic study, *130
- Krouse, H.: Psychopharmacologic study of schizophrenia and depressions; comparison of tolerance to sodium amytal and amphetamine sulfate, *372
- Kussmaul-Maier Disease: See Periarthritis nodosa
- Larynx, paralysis; early sign of recurrence following radical mastectomy for carcinoma, 429
- Lassek, A. M.: Human pyramidal tract; study of pyramids in cases of acute and chronic vascular lesions of brain, *339
- Lateral Sinus; anatomic variations of lateral and sigmoid sinuses, 150
- Laurence-Moon-Biedl Syndrome; abortive Fröhlich syndrome with disease of cerebellum and spinal cord, polydactyly and muscular atrophy; new syndrome (?), 432
- Legs: See Extremities
- Leopold, I. H.: Localizing value of temporal crescent defects in visual fields, *97
- Levulose; oxidation of fructose by brain in vitro, 306
- Lipoma, intracranial, 423
- Lissauer's Paralysis: See Dementia Paralytica
Tract: See Spinal Cord
- Little's Disease: See Paralysis, spastic
- Liver, pyridoxine deficiency in swine, with reference to anemia, epileptiform convulsions and fatty liver, 305
- Lobectomy: See Brain, surgery
- Lobotomy: See Brain, surgery
- Locomotion: See Movements
- Lotspeich, E. S.: Ependymitis and meningitis due to *Candida (Monilia) albicans*; report of fatal case of meningitis with comment on its clinical, bacteriologic and pathologic aspects, *361
- Louping Ill: See Encephalomyelitis
- Lungs: See Respiration; etc.
- Luse, S.: Electroencephalographic localization and differentiation of lesions of frontal lobes; pathologic confirmation, *197
- Lüys Body: See Hypothalamus
- Lymphogranuloma, Hodgkin's: See Hodgkin's Disease

- McCart, R. H.:** Changes in electrical activity of cortex due to applications of acetylcholine, 71
- Macrocephalosomia:** See Puberty, precocious
- Maler-Kussmaul Disease:** See Periarthritis nodosa
- Malaria, myasthenic syndrome occurring with,** 431
- Malnutrition:** See Vitamins; etc.
- Mammary Gland:** See Breast
- Man, E. B.:** Thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
- Mania:** See Insanity; Mental Diseases; etc.
- Mapharsen, Therapy:** See Syphilis
- Mastectomy:** See Breast
- Matthews, R. A.:** Psychologic factors in problem of obesity, 157
- Mecholyl:** See Choline and Choline Derivatives
- Medicine, Aviation:** See Aviation and Aviators
- Military:** See Military Medicine
- Naval:** See Naval Medicine
- new veteran and future for practice of,** 64
- Medin-Heine Disease:** See Poliomyelitis
- Medulla Oblongata, cavernous angioma of,** 310
- localizing value of vertical nystagmus,** *378
- Melancholia:** See Depression; Insanity
- Involuntal:** See Mental Diseases
- Memory, visual retention test for clinical use,** *212
- Ménière's Disease:** See Vertigo, aural
- Meninges, primary syphilis treated by 26 week course of mapharsen and bismuth; acute basilar meningitis with neuroretinitis developing during treatment,** 426
- Meningitis:** See also Meningococci and ependymitis due to *Candida* (Monilia) albicans; report of fatal case of meningitis with comment on its clinical, bacteriologic and pathologic aspects, *361
- chemotherapy of intracranial infections; treatment of staphylococcal and pneumococcal meningitis with sulfathiazole and sulfadiazine,** 222
- due to *Ps. pyocyanea*; penetrating wounds of head,** 222
- excretion of penicillin in spinal fluid in,** 62
- meningococcal,** 427
- meningococcal, and meningococcemia in childhood; statistical study of 72 cases,** 221
- meningococcal, in Santiago, Chile, 1941 to 1943; epidemic of 4,464 cases,** 221
- meningococcal; studies on 2-sulfamido-4-methylpyrimidine (sulfamerazine, sulfamethyldiazine) in man,** 429
- unilateral internal ophthalmoplegia; sole clinical sign in patient with syphilitic meningitis,** *389
- Meningococci:** See also under Meningitis
- acute meningococcal encephalomyelitis,** 221
- meningococcal meningitis and meningococcemia in childhood; statistical study of 72 cases,** 221
- Meningoencephalitis:** See Encephalitis; Meningitis
- Mental Diseases:** See also Children; Dementia Paralytica; Dementia Precox; Insanity; Neuroses and Psychoneuroses; Personality; Psychiatry; etc.
- arteriovenous aneurysm of midbrain and retina, facial nevi and mental changes,** 154
- common factors precipitating mental symptoms in aged,** 312
- convulsive shock therapy in involuntal states after complete failure with previous estrogenic treatment,** 307
- diethylstilbestrol in management of psychopathologic states in males,** 430
- immediate and follow-up results of electroshock treatment,** 424
- immediate circulatory and respiratory effects of convulsive shock,** 57
- incidence of advanced maternal age in mothers of 1,000 state hospital patients,** *186
- psychologic studies on patient who received 248 shock treatments,** *409
- "shock" therapies,** 425
- Mental Tests:** See also Memory; Personality
- chemotherapeutic prophylaxis with sulfonamide drugs; effect of small doses of sulfathiazole or sulfadiazine on mental efficiency and hand-eye coordination,** 425
- etiologic factors in adjustment of men in armed forces,** 309
- intellectual impairment in head injuries,** 220
- visual retention test for clinical use,** *212
- Merritt, H. H.:** Anticonvulsant activity of sulfoxides and sulfones, *319
- Experimental evidence of physiologic mechanism of certain types of headache,** *385
- Metabolism:** See also under specific headings, as Brain; etc.
- anorexia nervosa; metabolism and its relation to psychopathologic reactions,** 424
- Metals, sutureless reunion of severed nerves with elastic cuffs of tantalum,** 60
- Micturition:** See Urination
- Midbrain:** See Brain
- Migraine, capillaries of finger nail folds in cases of neurosis, epilepsy and migraine,** 225
- headaches relieved by hypoglycemic reaction,** 61
- Milhorat, A. T.:** Emotions and adrenergic and cholinergic changes in blood, *110
- Military Medicine:** See also Aviation and Aviators; Hospitals; Naval Medicine; Neuroses and Psychoneuroses; Recruits; Soldiers; Veterans; Wounds; etc.
- acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction,** *231
- chemotherapeutic prophylaxis with sulfonamide drugs; effect of small doses of sulfathiazole or sulfadiazine on mental efficiency and hand-eye coordination,** 425
- distinctive type of encephalomyelitis occurring among troops in northern territory of Australia,** 423
- gastrointestinal disorders,** 308
- management and treatment of craniocerebral injuries,** 433
- narcolepsy; combat experience of soldier with narcolepsy,** *367
- peptic ulcer in Canadian Army (1940-1944),** 429
- psychiatric aspects of injuries to nervous system,** 437
- rehabilitation of nervous system in war trauma,** 61
- review of cases of veterans of World War II discharged with neuropsychiatric diagnoses,** 424
- Mind, Diseases:** See Dementia Precox; Insanity; Mental Diseases; etc.
- Moniliais; ependymitis and meningitis due to *Candida* (Monilia) albicans; report of fatal case of meningitis with comment on its clinical, bacteriologic and pathologic aspects,** *361
- Moon-Laurence-Biedl Syndrome:** See Laurence-Moon-Biedl Syndrome
- Moriarty, J. D.:** Schizophrenic reaction syndrome in course of acute demyelination of central nervous system; clinicopathologic report of case, with brief review of literature, *202
- Morris, A. A.:** Ependymitis and meningitis due to *Candida* (Monilia) albicans; report of fatal case of meningitis with comment on its clinical, bacteriologic and pathologic aspects, *361
- Motion Sickness:** See Movements
- Motoneurons:** See Neurons
- Movements:** See also Muscles
- experimental production of motion sickness,** 421
- multiplicity of representation versus punctate localization in motor cortex; experimental investigation,** *256
- physiologic effects of bilateral simultaneous frontal lesions in primate,** 304
- Murphy, J. P.:** Multiplicity of representation versus punctate localization in motor cortex; experimental investigation, *256

Muscles, analysis of variability of spinal reflex thresholds, 419

Atrophy: See Atrophy, muscular
changes of weight and neuromuscular transmission in muscles of immobilized joints, 419

Dystrophy: See Dystrophy, muscular
electromyographic studies of muscle dysfunction in infectious polyneuritis and poliomyelitis, 60

Fatigue: See Fatigue
investigations on muscle atrophies arising from disuse and tenotomy, 421

Paralysis: See Paralysis
pyramidal section in cat, 421

studies on neuromotor systems of *Stylonychia pustulata* and *Stylonychia mytilus*, 305
tonus: paralysis with hypotonicity and hyperreflexia subsequent to section of basis pedunculi in monkeys, 218

tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175

Myasthenia Gravis, 152

changes in thymus with reference to, 422
myasthenic syndrome occurring with malaria, 431
prosgimine and ephedrine in, 62

Myelin: See under Brain; Nervous System; etc.

Myelitis: See also Encephalomyelitis
due to vaccination, 60

Myelography: See Spinal Canal Roentgenography

Myelopathy: See Spinal Cord

Myotonia Dystrophica: See Dystrophy, muscular

Nails, capillaries of finger nail folds in cases of neuroses, epilepsy and migraine, 225

Narcoanalysis: See Anesthesia

Narcolepsy: See under Sleep

Narcosis: See Anesthesia

Nares: See Nose

Nasopharynx, bilateral intracranial section of glossopharyngeal nerve; report of case, *344

Naval Medicine: See also Aviation and Aviators; Hospitals; Military Medicine; Recruits; etc.

enuresis in Navy, 424

problems of Naval psychiatry, 425

reactive anxiety and its treatment, 309

Negroes, partial albinism and nystagmus in, 156

Neoplasms: See Cancer; Tumors

Neostigmine: See Myasthenia Gravis

Nerves: See also Nervous System; Neuralgia;

Neuritis; Paralysis

Block: See Anesthesia

blood supply of sciatic nerve and its popliteal divisions in man, *283

Cells: See Neurons

changes of weight and neuromuscular transmission in muscles of immobilized joints, 419

embryonic grafts in regenerating tissue; development of dorsal and ventral ectoderm of *Rana pipiens gastrulae*, 417

extinction and precipitation of cutaneous sensations, *1

facial; distribution of myelinated afferent fibers in branches of cat's facial nerve, 304

fiber interaction in injured or compressed region of, 421

functional differentiation in embryonic development; cholinesterase activity of induced neural structures in *Amblystoma punctatum*, 418

glossopharyngeal, bilateral intracranial section of; report of case, *344

limb parameters and regression rates in denervated amputated limbs of urodele larvae, 419

Optic: See also Neuritis, optic

optic; congenital arterial aneurysm at papilla, 426

peripheral, blood supply; practical considerations, *280

peripheral, degeneration in pernicious anemia, *102

peripheral, effects of transient stretching of, *116

peripheral, recovery of fiber numbers and diameters in regeneration of, 306

Nerves—Continued

peripheral, use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of, 317

phases in regeneration of urodele limb and their dependence on nervous system, 417

roots; note on 2 components of dorsal root potential, 217

sutureless reunion of severed nerves with elastic cuffs of tantalum, 60

Nervous System: See also Brain; Cerebellum; Nerves; Neurons; Reflex; Spinal Cord; etc.

Blocking: See Anesthesia

central nervous system in diphtheria, 152

central nervous system in porphyria, 423

central nervous system in uremia; clinicopathologic study, *130

Diseases: See also Epilepsy; Mental Diseases; Neuritis; Neuroses and Psychoneuroses; etc.

diseases; effects of acetyl-beta-methylcholine in human subjects with localized lesions of central nervous system, 217

effects of penicillin on central nervous system, 160

parasympathetic regulation of high potential in electroencephalogram, 419

phases in regeneration of urodele limb and their dependence on, 417

polycythemia as neurosurgical problem; review, with reports of 2 cases, *25

psychiatric aspects of injuries to, 437

rehabilitation in war trauma, 61

review of some recent observations on demyelination, 219

schizophrenic reaction syndrome in course of acute demyelination of central nervous system; clinicopathologic report of case, with brief review of literature, *202

studies on neuromotor systems of *Stylonychia pustulata* and *Stylonychia mytilus*, 305

Surgery: See Brain, surgery; etc.

Syphilis: See Neurosyphilis

Nervousness: See Neuroses and Psychoneuroses

Neuralgia, bilateral intracranial section of glossopharyngeal nerve; report of case, *344

fiber interaction in injured or compressed region of nerve, 421

post-traumatic pain and causalgic syndrome, 61

traumatic glossopharyngeal, 160

Neuritis, electromyographic studies of muscle dysfunction in infectious polyneuritis and poliomyelitis, 60

multiple peripheral neuritis occurring with sulfonamide therapy, 60

optic; binocular papilledema in case of torulosis associated with Hodgkin's disease, 426

optic; polycythemia as neurosurgical problem; review, with reports of 2 cases, *25

optic; primary syphilis treated by 26 week course of mapharsen and bismuth; acute basilar meningitis with neuroretinitis developing during treatment, 426

Neurofibromatosis and myasthenia gravis, 152

diffuse (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223

Neurohypophysis: See Pituitary Body

Neurology: See Nerves; Nervous System; Neuropsychiatry; Neuroses and Psychoneuroses; etc.

Neurons, human pyramidal tract; study of pyramids in cases of acute and chronic vascular lesions of brain, 339

Neuropsychiatry: See also Military Medicine; Naval Medicine; Psychiatry; War; etc.

conference on neuropsychiatry by members of Medical Corps, Ninth Service Command, 412

review of cases of veterans of World War II discharged with neuropsychiatric diagnoses, 424

tropical, 308

Neuroses and Psychoneuroses: See also Mental Diseases; Nervous System, diseases; etc.

acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231

- Neuroses and Psychoneuroses—Continued
 capillaries of finger nail folds in cases of neurosis, epilepsy and migraine, 225
 civilian war neuroses and their treatment, 152
 delayed and favorable effects in psychotherapy, 158
 neurotic manifestations of voice, 307
 physical examination of 2000 cases of neurosis, 153
 psychoneuroses of war, 220
 reactive anxiety and its treatment, 309
 some aspects of compulsion neurosis in changing civilization, 307
 tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
- Neurosurgery: See Brain, surgery
- Neurosyphilis: See also Dementia Paralytica
 artificially induced fever as therapeutic procedure, 431
- Nevi, arteriovenous aneurysm of midbrain and retina, facial nevi and mental changes, 154
- Newborn Infants: See Infants, newborn
- Neymann, C. A.: Experimental study on treatment of dementia paralytica with penicillin, 311
- Nissl Granules: See Neurons
- Nitrogen, water and electrolyte concentration in brain, 306
- Nose: See also Nasopharynx
 discharge; treatment of rhinorrhea and otorrhea, 430
- Nucleus Dentatus: See under Cerebellum
- Lateralis Medullae: See Medulla Oblongata
- Pulposus: See Spine, intervertebral disks
- Nutrition: See Dystrophy; Vitamins
- Nycturia: See Urination, incontinence
- Nystagmus: See also Cerebellum
 and partial albinism in Negroes, 156
 unusual forms of, 309
 vertical, localizing value of, *378
- Obesity: See also under Laurence-Moon-Biedl Syndrome; Pituitary Body
 psychologic factors in problem of, 157
- OBITUARIES:
- Jelliffe, Smith Ely, 301
- del Rio-Hortega, Pio, 413
- Sittig, Otto, 303
- O'Brien, F. H.: Localizing value of vertical nystagmus, *378
- Obsessions: See Dementia Precox; Neuroses and Psychoneuroses
- Occipital Bone; platybasia (basilar impression) secondary to advanced osteitis deformans (Paget's disease), with severe neurologic manifestations; successful surgical result; report of case, 68
- Odontoid Process: See Atlas and Axis
- Old Age; common factors precipitating mental symptoms in aged, 312
- Oligodendroglioma, disseminated, *274
- Olivary Body: See Medulla Oblongata
- Olkon, D. M.: Psychiatric problems presented by inductee and soldier, 63
- Ophthalmoplegia: See Eyes, paralysis
- Optic Disk: See Nerves, optic
- Choked: See Neuritis, optic
- Optic Papilla: See Nerves, optic
- Osteitis deformans; platybasia (basilar impression) secondary to advanced osteitis deformans (Paget's disease) with severe neurologic manifestations; successful surgical result; report of case, 68
- fibrosa; syndrome of precocious puberty, fibrocystic bone disease and pigmentation of skin; 11 years' observation of case, 310
- Otorrhea: See Ear, discharge
- Oxidation: See Acid, lactic
- Oxygen: See also Respiration
 deficiency; effect of anoxia on vestibular apparatus, 305
 deficiency; responses of schizophrenic patients to induced anoxia, 307
 experimental edema of brain; cerebral circulation, 307
- Paget's Disease of Bones: See Osteitis deformans
- Pain: See also Sensation
 neurosurgery and radiation for relief in advanced cancer, 431
 structural identity of pain spot in human skin, 150
- Palsy: See Paralysis
- Pantopaque: See Spinal Canal Roentgenography
- Papilledema: See Neuritis, optic
- Parachutists: See Aviation and Aviators
- Paralysis: See also Eyes, paralysis; Hemiplegia; Larynx, paralysis; Poliomyelitis
 agitans; tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
 flaccid; relations of cerebral cortex to spasticity and flaccidity, 420
 General: See Dementia Paralytica
 Infantile: See Poliomyelitis
 Laryngeal: See Larynx, paralysis
 progressive ascending, in dogs due to deficiency of vitamin B complex factor found in yeast, 151
 spastic; relation of cerebral cortex to spasticity and flaccidity, 420
 with hypotonicity and hyperreflexia subsequent to section of basis pedunculi in monkeys, 218
- Paranola: See Dementia Precox
- Paresis: See Dementia Paralytica
- Parietal Bone; developmental thinness of, 224
- Parietal Lobe: See Brain
- Parkinsonism: See Encephalitis; Paralysis, agitans
- Pavlov; acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
- Pearson, G. H. J.: "Acting out" as defense mechanism; report of case, 159
- Penfield, W.: Pio del Rio-Hortega, 413
- Penicillin, effects on central nervous system, 160
 excretion in spinal fluid in meningitis, 62
 Therapy: See Dementia Paralytica; Meningitis
- Pentothal: See Anesthesia
- Peptic Ulcer; gastroduodenal disorders, 308
 in Canadian Army (1940-1944), 429
- Perception: See Sensation; etc.
- Periarthritis nodosa; cerebral thromboangitis obliterans and its relation to, 219
- Perimetry: See Vision
- Perlson, J.: Psychologic studies on patient who received 248 shock treatments, *409
- Personality, study of 40 male psychopathic personalities before, during and after hospitalization, 424
- Perspiration: See under Sweat Glands
- pH: See Hydrogen Ion Concentration
- Phobias: See Neuroses and Psychoneuroses
- Physical Examination of 2000 cases of neurosis, 153
- Pia Mater: See also Meninges
 pial circulation and spreading depression of activity in cerebral cortex, 306
- Pigmentation: See also Nevi
 syndrome of precocious puberty, fibrocystic bone disease and pigmentation of skin; 11 years' observation of case, 310
- Pineal Gland, cystic hydrops of, 427
- Pituitary Body: See also Hypothalamus
 abortive Fröhlich syndrome with disease of cerebellum and spinal cord, polydactyly and muscular atrophy; new syndrome (?), 432

- Pituitary Body**—Continued
 cavernous sinus thrombophlebitis; report of case with multiple cerebral infarcts and necrosis of pituitary body, 153
 inhibition of histamine release by pituitary-adrenal mechanism, 422
 Simmonds' disease with therapeutic response to hormone therapy for 4 years; report of case with necropsy findings, 151
- Plasmodium**: See Malaria
- Platybasia**: See Atlas and Axis; Occipital Bone
- Pneumocephalus**, traumatic, with spontaneous ventriculograms, 58
- Pneumococci**: See also under Meningitis
 chemotherapy of intracranial infections; treatment of staphylococci and pneumococci meningitis with sulfathiazole and sulfadiazine, 222
- Pneumonia**, encephalitis complicating virus pneumonia, 151
- Poisons and Poisoning**: See under names of various substances, as Bromide and Bromine; Chloroform; etc.
- Polioencephalitis**: See Encephalitis
- Polioencephalomyelitis**: See Encephalomyelitis
- Poliomyelitis**: See also Encephalomyelitis
 and tonsillectomy; 1 case of poliomyelitis following 8,915 tonsillectomies, 60
 attempts to recover virus from fruit, well water, chicken cords and dog stools, 429
 convalescent; pathology in man, 422
 effect of activated sludge process of sewage treatment on virus, 428
 electromyographic studies of muscle dysfunction in infectious polyneuritis and poliomyelitis, 60
 salt metabolism in, 57
- Pollock, L. J.**: Use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of peripheral nerves, 317
- Polycythemia** as neurosurgical problem; review, with reports of 2 cases, *25
- Polydactylia**: See Laurence-Moon-Biedl Syndrome
- Polyneuritis**: See under Neuritis
- Polyopia and monocular diplopia of cerebral origin**, *323
- Popliteal Space**; blood supply of sciatic nerve and its popliteal divisions in man, *283
- Forencephaly**: See Brain, cysts
- Porphyrin and Porphyrin Compounds**; central nervous system in porphyria, 423
- Position**: See Posture
- Posture**; paroxysmal and postural headaches from intraventricular cysts and tumors, 155
- Prados, M.**: Studies on cerebral edema; reaction of brain to air exposure; pathologic changes, *163
 Studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290
- Pregnancy**, incidence of advanced maternal age in mothers of 1,000 state hospital patients, *186
- Prostigmene**: See Myasthenia Gravis
- Pseudomonas**: See Bacteria, pyocyanus
- Psychiatry**: See also Hospitals; Insanity; Mental Diseases; Neuropsychiatry; Psychoanalysis; Psychotherapy; War; etc.
 new veteran and future for practice of medicine, 64
 postgraduate course, McGill University, 412
 problems of Naval psychiatry, 425
 psychiatric aspects of injuries to nervous system, 437
 psychiatric problems presented by inductee and soldier, 68
 University of California course in, 412
- Psychoanalysis**: See also Psychotherapy
 "acting out" as defense mechanism; report of case, 159
 civilian war neuroses and their treatment, 152
 some aspects of compulsion neurosis in changing civilization, 307
 sublimation, 220
- Psychology**: See Memory; Mental Tests; Personality; War; etc.
- Psychoneuroses**: See Neuroses and Psychoneuroses
- Psychoses**: See Insanity; Mental Diseases; Neuroses and Psychoneuroses; etc.
- Psychotherapy**: See also Psychoanalysis
 and public education, 159
 civilian war neuroses and their treatment, 152
 delayed favorable effects in, 158
 group psychotherapy in mental institutions, 64
 hysterical convulsions treated with hypnosis and psychotherapy; report of case, 314
- Puberty, precocious**; syndrome of precocious puberty, fibrocystic bone disease and pigmentation of skin; 11 years' observation of case, 310
- Pupillotonia**: See Reflex, pupillary
- Putnam, T. J.**: Anticonvulsant activity of sulfoxides and sulfones, *319
- Pyramidal Tract, human**; study of pyramids in cases of acute and chronic vascular lesions of brain, *339
 pyramidal section in cat, 421
- Pyrexia**: See Fever
- Pyridoxine**: See also Vitamins, B
 deficiency in swine, with reference to anemia, epileptiform convulsions and fatty liver, 305
- Races**: See Negroes; etc.
- von Recklinghausen's Disease**: See Neurofibromatosis; Osteitis fibrosa
- Reconditioning**: See Rehabilitation
- Recruits**: See also Military Medicine
 enuresis in Navy, 424
 psychiatric problems presented by inductee and soldier, 68
- Reflex, acute war neurosis**; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
 analysis of variability of spinal reflex thresholds, 419
- Carotid**: See Carotid Sinus
 paralysis with hypotonicity and hyperreflexia subsequent to section of basis pedunculi in monkeys, 218
 pupillary; afferent path of pupillodilator reflex in cat, 418
 reactions of monkeys of various ages to partial and complete decortication, 57
- Rehabilitation**: See also Hospitals; Military Medicine; Neuroses and Psychoneuroses; Soldiers; Veterans; etc.
 new veteran and future for practice of medicine, 64
- Respiration, immediate circulatory and respiratory effects of convulsive shock**, 57
 variation in circulatory and respiratory responses to carotid sinus stimulation in man, 418
- Restiform Body**: See Medulla Oblongata
- Retina, Aneurysm**: See Aneurysm
 Inflammation: See Retinitis
- Retinitis, primary syphilis treated by 26 week course of mapharsen and bismuth**; acute basilar meningitis with neuroretinitis developing during treatment, 426
- Rheumatic Fever, late cerebral sequelae of**, 151
- Rhinorrhea**: See Nose, discharge
- Ribs, abnormalities, roentgenologic manifestations and clinical symptoms of**, 224
- Roentgen Rays, Therapy**: See under names of organs, regions and diseases
- Roizln, L.**: Schizophrenic reaction syndrome in course of acute demyelination of central nervous system; clinicopathologic report of case, with brief review of literature, *202
- Rorschach Test**: See Mental Tests; Personality
- Roussy-Dejerine Syndrome**: See Thalamus

- Sacroccocygeal Region**: chordomata; review of literature, with report of sacroccocygeal case, 59
- Sailors**: See Naval Medicine; etc.
- Sanarelli-Shwartzman Phenomenon**: See Shwartzman Phenomenon
- Sargant, W.**: Acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
- Scarlet Fever**: allergic brain changes in post-scarlatinal encephalitis, 152
- Scheinker, I. M.**: Changes in cerebral veins in hypertensive brain disease and relation to cerebral hemorrhage; clinical pathologic study, *395
- Schizophrenia**: See Dementia Precox
- Schopbach, R. R.**: Psychological factors in problem of obesity, 157
- Sclerosis, multiple, acute**, 428
multiple, with late onset of symptoms, *348
- Selective Service**: See Recruits
- Senile Plaque**: See Sclerosis
- Senility**: See Old Age
- Sensation**: See also Pain; etc.
extinction and precipitation of cutaneous sensations, *1
receiving areas of tactile, auditory and visual systems in cerebellum, 217
- Sewage**, effect of activated sludge process of sewage treatment on poliomyelitis virus, 428
- Sex, Precocious Development**: See Puberty, precocious
- Shenkin, H. A.**: Localization value of temporal crescent defects in visual fields, *97
- Shock, Electric**: See Dementia Precox; Electrotherapy; Epilepsy; Mental Diseases; etc.
Emotional: See Emotions
- Shorvon, H. J.**: Acute war neurosis; special reference to Pavlov's experimental observations and mechanism of abreaction, *231
- Shwartzman Phenomenon**: general Sanarelli-Shwartzman phenomenon with fatal outcome following typhoid vaccine therapy, 430
- Sigmoid Sinus**: See Lateral Sinus
- Simmonds' Disease**: See under Pituitary Body
- Sinus, Lateral**: See Lateral Sinus
- Sigmoid**: See Lateral Sinus
- Thrombosis**: See Thrombosis
- Skeleton**: See Bones
- Skin**: See also Sensation
diseases; diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
extinction and precipitation of cutaneous sensations, *1
structural identity of pain spot in human skin, 150
- Skull**: See Cranium
- Sleep**, disturbances in sleep mechanism; clinico-pathologic study; lesions at corticodiencephalic level, *241
narcolepsy; combat experience of soldier with narcolepsy, *367
- Sleeping Sickness**: See Encephalitis
- Smallpox**, myelitis due to vaccination, 60
- Social Hygiene**; American Sociometric Association, 74
- Societies, American Psychiatric Association**, 74
American Sociometric Association, 74
Association for Research in Nervous and Mental Diseases, 230
- SOCIETY TRANSACTIONS**:
Boston Society of Psychiatry and Neurology, 225
Chicago Neurological Society, 160, 317
Cincinnati Society of Neurology and Psychiatry, 229
- SOCIETY TRANSACTIONS—Continued**
Illinois Psychiatric Society, 64, 311
New York Neurological Society and New York Academy of Medicine, Section of Neurology and Psychiatry, 433
Philadelphia Neurological Society, 68, 226
Philadelphia Psychiatric Society, 157
- Sodium Amytal**: See Barbitol and Barbitol Derivatives
- Diphenylhydantoinate**: See Epilepsy
- Soldiers**: See also Military Medicine; Neuroses and Psychoneuroses; etc.
psychiatric problems presented by inductee and soldier, 68
- Sommer, C.**: New veteran and future for practice of medicine, 64
- Somnolence**: See Sleep
- Space, perception**; polyopia and monocular diplopia of cerebral origin, *323
- Spaeth, E. B.**: Acute cortical blindness with recovery: report of case, 70
- Spasm**: See Convulsions; Epilepsy; etc.
- Spinal Canal Roentgenography**: See also Spinal Cord
myelography with pantopaque and new technic for its removal, 431
- Spinal Cord**: See also Meninges; Nervous System; Pyramidal Tract; etc.
abortive Fröhlich syndrome with disease of cerebellum and spinal cord, polydactyly and muscular atrophy; new syndrome (?), 432
curious lesions of; report of 2 cases, 226
extinction and precipitation of cutaneous sensations, *1
extradural hemorrhage; report of case, 161
Inflammation: See Myelitis
- Spinal Fluid**: See Cerebrospinal Fluid
- Spine**: See also Atlas and Axis
abnormalities; Klippel-Feil malformation, 63
intervertebral disks; brachial pain from herniation of cervical intervertebral disk, 60
intervertebral disks, pathology, clinical manifestations and treatment of lesions of, 59
intervertebral disks; recent advances in treatment of ruptured (lumbar) intervertebral disks, 428
- Staphylococci**, chemotherapy of intracranial infections; treatment of staphylococcal and pneumococcal meningitis with sulfathiazole and sulfadiazine, 222
- Status Epilepticus**: See under Epilepsy
- Stilbestrol**: See Estrogens
- Stomach, Ulcers**: See Peptic Ulcer
- Stools**: See Feces
- Striae Medullaris**: See Brain
- Strowger, B.**: Studies on cerebral edema; reaction of brain to air exposure; pathologic changes, *163
Studies on cerebral edema; reaction of brain to exposure to air; physiologic changes, *290
- Subarachnoid Space**: See Meninges
- Subdural Spaces**: See Meninges
- Sublimation**: See Psychoanalysis
- Substantia Nigra**: See Brain
- Subthalamus**: See Hypothalamus
- Sugar**: See Dextrose
- Sulfadiazine**: See Meninges; Sulfonamides; etc.
- Sulfonamides**, chemotherapeutic prophylaxis with sulfonamide drugs; effect of small doses of sulfathiazole or sulfadiazine on mental efficiency and hand-eye coordination, 425
multiple peripheral neuritis occurring with sulfonamide therapy, 60
studies on 2-sulfamido-4-methyl-pyrimidine (sulfamerazine, sulfamethyldiazine) in man; treatment of meningococcal meningitis, 429
Therapy: See Meningitis; etc.
- Sulfones**, anticonvulsant activity of sulfoxides and sulfones, *319

- Sulfur, anticonvulsant activity of sulfoxides and sulfones, *319
- Sunderland, S.: Blood supply of peripheral nerves; practical considerations, *280
Blood supply of sciatic nerve and its popliteal divisions in man, *283
- Suprarenal Preparations: See Adrenal Preparations
- Suprenalectomy: See under Adrenals
- Suprenals: See Adrenals
- Surgery: See under organs and regions, as Brain, surgery; Spinal Cord; etc.
- Sweat Glands: studies on palmar sweating, 217
- Syphilis: See also Neurosyphilis; and under names of organs and regions, as Meninges; etc.
early; hemorrhagic encephalopathy following 5 day treatment with massive doses of oxophenarsine hydrochloride (mapharsen); report of case with recovery, 65
primary, treated by 26 week course of mapharsen and bismuth; acute basilar meningitis with neuroretinitis developing during treatment, 426
- Tabes Dorsalis: See also Neurosyphilis
aspects of, 429
tabetic arthropathy of hip, 62
- Tantalum: See Metals
- Tetanus: use of galvanic tetanus and galvanic tetanus ratios in electrodiagnosis of lesions of peripheral nerves, 317
- Thalamus: Dejerine-Roussay syndrome caused by gunshot wound; report of case, 223
hypothalamic attacks with thalamic lesion; anatomic considerations, *44
hypothalamic attacks with thalamic lesion; physiologic and psychologic considerations, *37
- Thiamine: See also Vitamins, B
lactic acid oxidation quotient in minced brain of normal and avitaminotic chicken, 418
- Thorax: See Ribs; etc.
- Throat: See also Larynx; etc.
pain; bilateral intracranial section of glossopharyngeal nerve; report of case, *344
- Thromboangiitis Obliterans, cerebral, and its relation to periarteritis nodosa, 219
- Thrombophlebitis, Sinus: See Thrombosis
- Thrombosis, cavernous sinus thrombophlebitis; report of case with multiple cerebral infarcts and necrosis of pituitary body, 153
localizing value of vertical nystagmus, *378
porencephaly; studies in phlebothrombosis and phlebostasis, 219
- Thymoma and myasthenia gravis, 152
- Thymus, changes with reference to myasthenia gravis, 422
- Thyroid function of manic-depressive patients evaluated by determinations of serum iodine, *51
- Tissue, determination of carbonic anhydrase in human autopsy tissue, 306
embryonic grafts in regenerating tissue; development of dorsal and ventral ectoderm of *Rana pipiens* gastrulae, 417
- Tocopherol: See Vitamins, E
- Tonsillectomy and poliomyelitis; 1 case of poliomyelitis following 8,915 tonsillectomies, 60
- Torticollis, spasmodic, 154
- Torulosis, binocular papilledema in case of torulosis associated with Hodgkin's disease, 426
- Toxoplasmosis; report of ocular findings in infant twins, 223
- Tractus Solitarius: See Medulla Oblongata
- Transfusion: See Blood transfusion
- Transplantation: See Nerves
- Trauma: See also under Brain; Cranium; Extremities; Head; etc.
mechanics with reference to herniation of cerebral tissue, 57
traumatic glossopharyngeal neuralgia, 160
- Tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
- Tropical Medicine; tropical neuropsychiatry, 308
- Tuber Cinereum: See Hypothalamus
- Tuberculosis: See under names of organs, regions and diseases
- Tuberculum Sellae: See Hypothalamus
- Tumors: See also Angioma; Astrocytoma; Choroidoma; Lipoma; Oligodendroglioma; and under names of organs and regions, as Brain; etc.
metastasis; spinal fluid in metastatic brain tumors, 223
- Twins, diffuse neurofibromatosis (von Recklinghausen's disease) involving bulbar conjunctiva; report of case, with lesions of skeletal system and skin, bodily asymmetry and intracranial involvement, 223
toxoplasmosis; report of ocular findings in infant twins, 223
- Typhoid; general Sanarelli-Schwartzman phenomenon with fatal outcome following typhoid vaccine therapy, 430
- Ulcers, Peptic: See Peptic Ulcer
- Ulett, G.: Electroencephalogram of dogs with experimental space-occupying intracranial lesions, *141
- Unconscious: See Psychoanalysis
- Uremia, central nervous system in; clinicopathologic study, *130
- Urination, incontinence; enuresis in Navy, 424
- Ury, B.: Hysterical convulsions treated with hypnosis and psychotherapy; report of case, 314
- Vaccination: See Smallpox
- Encephalitis Following: See under Encephalitis
- Variola: See Smallpox
- Vasomotor System: See also Arteries; Capillaries; Nervous System; Veins
one aspect of post-traumatic syndrome in cranio-cerebral injuries, 223
- Veins: See also Thrombosis; Vasomotor System
cerebral; changes in cerebral veins in hypertensive brain disease and relation to cerebral hemorrhage; clinical pathologic study, *395
Pressure in: See Blood pressure
- Veneral Diseases: See Neurosyphilis; Syphilis; etc.
- Verbruggen, A.: Extradural hemorrhage; report of case, 161
- Vertebrae: See Atlas and Axis; Spine
- Vertigo, aural; Ménière's syndrome; comparison of results of medical and surgical treatment, *192
- Vestibular Apparatus: See Ear
- Nuclei: See Medulla Oblongata
- Veterans; new veteran and future for practice of medicine, 64
review of cases of veterans of World War II discharged with neuropsychiatric diagnoses, 424
- Viruses: See Pneumonia; Poliomyelitis
- Vision: See also Blindness
after-image perimetry; rapid method of obtaining visual fields; preliminary report, 427
localizing value of temporal crescent defects in visual fields, *97
polyopia and monocular diplopia of cerebral origin, *323
visual retention test for clinical use, *212
- Vitamins: See also Pyridoxine; Thiamine; etc.
B; progressive ascending paralysis in dogs due to deficiency of vitamin B complex factor found in yeast, 151
B₁: See Thiamine
B₆: See Pyridoxine
E; defect in utilization of tocopherol in progressive muscular dystrophy, 218
- Vocal Cords, Paralysis: See Larynx, paralysis

- Voice, neurotic manifestations of, 307
- Voris, H. C.: Traumatic glossopharyngeal neuralgia, 160
- Walker, A. E.: Effects of penicillin on central nervous system, 160
- War: See also Aviation and Aviators; Hospitals; Military Medicine; Naval Medicine; Soldiers; Veterans; Wounds; etc.
psychoneuroses of, 220
tremors of combat neuroses; comparison with tremors of paralysis agitans, delirium tremens and psychoneuroses of civilian life; electromyographic studies, *175
- Wartenberg, R.: Progressive facial hemiatrophy, *75
- Water, attempts to recover poliomyelitis virus from fruit, well water, chicken cords and dog stools, 429
nitrogen and electrolyte concentration in brain, 306
- Well, A. A.: Schizophrenic reaction syndrome in course of acute demyelination of central nervous system; clinicopathologic report of case, with brief review of literature, *202
- Willis, Circle of: See Brain
- Wounds: See also Military Medicine; Naval Medicine; War
Dejerine-Roussy syndrome caused by gunshot wound; report of case, 223
rehabilitation of nervous system in war trauma, 61
- Wycis, H.: Bilateral intracranial section of glossopharyngeal nerve; report of case, *344
Platybasia (basilar impression) secondary to advanced osteitis deformans (Paget's disease), with severe neurologic manifestations; successful surgical result; report of case, 68
- Yaskin, J. C.: Acute cortical blindness with recovery; report of case, 70
Delayed favorable effects in psychotherapy, 158
- Yeager, C. L.: Electroencephalographic localization and differentiation of lesions of frontal lobes; pathologic confirmation, *197
- Yeast: See Vitamins, B
- Youmans, G. P.: Experimental study on treatment of dementia paralytica with penicillin, 311
- Zelligs, M. A.: Unilateral internal ophthalmoplegia; sole clinical sign in patient with syphilitic meningitis, *389

